

Review

Integrative Nutritional Therapy in Canine Cancer

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ABSTRACT

In humans and animals, diet is an important aspect of cancer prevention and treatment. Although the research in this area is primarily in humans, studies have demonstrated that dietary therapy may be helpful in preventing or slowing the development of canine cancer and in supporting patients receiving standard care. In an integrative nutritional approach, the conventional therapy consists of specially designed diets that may include whole food items, probiotics, vitamins, fatty acids, and natural polyphenols. These can be custom designed to select for efficacy against particular cancer types and organ protection during toxic cancer treatments. Along with conventional therapy, the addition of traditional Chinese medicine and Chinese food therapy benefits modern clinical treatment with knowledge gleaned over several thousand years by Chinese physicians. For example, the herb *Qing Hao* (*Artemisia*) has anti-cancer effects in canine osteosarcoma cell lines and has also been seen to increase survival in small animal cancer patients. *Gan Jiang* (dry Ginger) has lessened the incidence of emesis in cisplatin-treated dogs. It is possible with consideration of knowledge from human literature, both ancient and modern, that syndrome differentiation in Chinese food therapy combined with conventional nutritional therapy, helps improve quality of life and may lengthen survival in canine patients with cancer.

Keywords: cancer, canine cancer, Chinese food therapy, diet, dietary therapy, nutritional therapy, traditional Chinese veterinary medicine

ABBREVIATIONS: 25(OH)D: 25-hydroxyvitamin D; ALT: alanine aminotransferase; CCNU: lomustine; CE: Common Era - secular equivalent of AD (anno Domini); CFT: Chinese food therapy; CHM: Chinese herbal medicine; CYLD: cylindromatosis lysine 63 deubiquitinase; DFI: disease-free interval; DHA: docosahexaenoic acid; EPA: eicosapentaenoic acid; HDAC: histone deacetylase; IGF-1: insulin-like growth factor 1; KMT: ketogenic metabolic therapy; PLD: pegylated liposomal doxorubicin; PPES: palmar-plantar erythrodysesthesia; PSp: polysaccharide extract of *Spirulina platensis*; PSP: polysaccharopeptide; PUFA: polyunsaturated fatty acid; SAME: S-adenosylmethionine; SCFA: short chain fatty acid; SNP: polysaccharide extract of *Sipunculus nudus*; TCM: traditional Chinese medicine; TCVM: traditional Chinese veterinary medicine; YBY: *Yunnan Bai Yao*

Improvements in medicine and nutrition have led to an increased canine and feline lifespan.^{1,2} As a result, with longer survival, there is an increased risk of developing cancer. In the process of evolution, species have acquired cancer-protective mechanisms that are associated with energy demands, reproductive strategies, and expected lifespan.² In cases of rapid increases in longevity, these mechanisms may be incapable of providing cancer protection. According to the literature, other factors that may influence the prevalence of cancer in companion animals include diet, body condition score, sterilization practices, tap water contaminants, airborne environmental pollutants, insecticide use, and inflammation induced by vaccines or other injections.³⁻⁷ It is believed that cancer is one of the most common causes of death in dogs and humans in the developed world, with an estimated 1 in 4 canines diagnosed with cancer in their lifetime.² In contrast, it is uncommon in wildlife species that have been studied, such as marine mammals and birds.

In multicellular animals, a neoplasm arises from malignant transformation of a single cell that continues to proliferate.² The somatic changes leading to inappropriate

cell division or survival include mutations, changes in the number of copies of chromosomal segments, and epigenetic structural changes causing oncogenic activation.^{2,8} Some of the epigenetic changes are aberrant DNA methylation, histone modifications, and microRNA (miRNA) expression.⁹ These somatic changes together with a failure of cancer protective mechanisms allow cells to proliferate.² It is suggested that any compound that benefits these changes may lead to increased risk of cancer. In addition, the transformed cells need a permissive environment in which to grow and develop into a neoplasm. It is proposed that aging and related cellular senescence, proinflammation, and waning immunity allow a permissive environment to arise, leading to cancer development in an animal.²

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CONVENTIONAL TREATMENT

In cancer, conventional medicine may include surgery, chemotherapy, radiation therapy, or immunotherapy, depending on the type of neoplasia present.¹⁰ It is focused on treating the disease (i.e. killing cancer cells) as opposed to a more holistic therapy (making the microenvironment inhospitable to cancer cells). With its direct approach of killing cancer cells, conventional medicine can cause side effects and complications, ranging from mild to severe.¹⁰⁻¹² In addition, chemotherapy may fail if resistant cells emerge.¹³ It is suggested that some canine cancer cells have intrinsic or acquired mechanisms of resistance, such as increased rates of chemotherapeutic efflux, enhanced DNA repair systems, or inhibition of apoptosis.^{14,15}

A unique approach to the clinical problem of resistant cancer cells, is their elimination through cell-mediated immunotherapy.¹³ Often cancer patients have compromised immune systems.¹⁶ As an example, dogs with lymphosarcoma or osteosarcoma may have a decrease in circulating T cells, thus allowing cancer development and progression.^{16,17} In addition, circulating immune complexes may be present in dogs with mammary carcinoma that seem to impede the immune response.¹⁶ Evidence is accumulating that immunotherapy may help to increase survival and quality of life in some patients, and may provide long-term protection due to immune memory.^{13,18,19}

Supportive Therapy

In canine cancer patients, supportive therapy can provide a number of benefits. As an example, capromorelin may be helpful to treat inappetence or weight loss related to chemotherapy or chronic illness in cats and dogs.²⁰⁻²² It is a small molecule that mimics the action of ghrelin, causing an increase in appetite and secretion of insulin-like growth factor 1 (IGF-1); however, it may have side effects in some dogs, and it is unclear whether an increase in IGF-1 will affect the clinical progression of cancer in dogs. Studies in human medicine support its use with a favorable safety profile for ghrelin or ghrelin receptor agonist therapy in cancer cachexia.^{22,23} Other supportive therapies include mirtazapine for appetite loss, and crofelemer, an extract from the *Croton lechleri* tree, which is used in treating chemotherapy-induced diarrhea in dogs.^{22,24,25}

CONVENTIONAL NUTRITIONAL THERAPY

Diets and Nutritional Supplements

It is suggested that nutrition has a beneficial effect in improving survival time and quality of life in cancer patients.²⁶⁻²⁸ A diet based on plant and fish proteins, healthful fats, and carbohydrates from unrefined whole grains, vegetables, and fruits is supported in human cohort studies.²⁹ Special diets, including supplements, designed to help prevent and treat canine cancer may be beneficial to include in an integrative medical treatment (Box 1).

A therapeutic diet may benefit caloric intake and appropriate weight gain in canines with various types of cancer.³⁰ A poor appetite along with loss of muscle mass or cachexia may be present in dogs living with cancer.^{30,31} It is reported that a loss of body weight is related to shortened survival indices in lymphoma.^{32,33} In a single-arm multicenter prospective study, a calorically dense therapeutic diet^a was seen to increase food intake in both grams and calories in dogs with malignancies.³⁰ The diet was also shown to significantly increase body weight and body fat index ($p < 0.0001$ and $p = 0.0232$ in dogs with malignant disease, respectively). According to Anthony et al., an increase in body weight along with body fat indicates a positive energy balance and is likely to help spare lean muscle mass. The findings in this study suggest that the therapeutic diet may be helpful to nutritionally support dogs diagnosed with malignancy.

Foods containing phytonutrients including carotenoids may help lessen the risk of canine transitional cell tumor of the bladder.³⁴ Carotenoids are lipid soluble natural pigments in green and yellow-orange vegetables that may lessen cell proliferation and transformation.³⁴⁻³⁶ In some studies, an increase in dietary intake of carotenoids has been related to a lower risk of bladder cancer in humans.^{35,36} In a study by Raghavan et al., it was found that consumption of any type of vegetable at least 3 times a week was associated with a significantly decreased risk of developing transitional cell carcinoma of the urinary bladder in a population of Scottish terriers ($p = 0.001$).³⁴ Specifically, consumption of yellow-orange vegetables, such as carrots, sweet potatoes, and yellow squash, at least 3 times a week was seen to lessen the risk of developing transitional cell carcinoma ($p = 0.005$). The study findings suggest that there are potential cancer-preventive benefits related to consuming certain vegetables in dogs.

Ketogenic metabolic therapy (KMT) is emerging as a nutritional intervention in cancer patients.^{37,38} It utilizes a diet that limits fermentable fuels and increases levels of fatty acids and ketone bodies.³⁷ It is proposed that KMT may be helpful to lessen aerobic glucose fermentation used in the growth of cancer cells. In a case study, a 7-year-old female Pit Bull Terrier with a cutaneous mast cell tumor under the right nostril was treated with KMT as a sole therapy.³⁷ Initially, the diet was changed from an over-the-counter product to raw vegetables and cooked fish, but the tumor continued to progress. The patient was subsequently transitioned to a raw, calorie restricted, ketogenic diet consisting of chicken, eggs, and coconut/pollock oils. A raw radish was given as a treat between each meal. The tumor gradually disappeared over the following few months and the patient maintained an attentive and active behavior. There was no apparent recurrence over the following 6 years, and the patient passed away without pain from an unrelated issue. A ketogenic diet may help to limit progression in some canine malignancies.

A diet supplemented with menhaden fish oil (n-3 fatty acids) and arginine may be used to help improve metabolic

health parameters and survival in dogs with lymphoma.²⁶ It is reported that polyunsaturated n-3 fatty acids may enhance the immune system and decrease tumorigenesis, metastasis, and the occurrence of cachexia in animal models.^{26,39} The amino acid arginine has been seen to improve the immune response in humans.⁴⁰ In a double-blind randomized placebo-controlled study, a diet containing these ingredients was shown to significantly increase serum levels of the n-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) as well as plasma arginine in dogs with lymphoblastic lymphoma given doxorubicin chemotherapy ($p < 0.05$).²⁶ This diet was also seen to lessen the concentration of plasma lactic acid in response to an intravenous glucose tolerance test ($p < 0.05$). Of interest, an elevation in blood lactic acid is a consistent finding in dogs with malignant disease and is associated with cancer cachexia.²⁶ In dogs with stage III lymphoma given the experimental diet, increased DHA and arginine levels were significantly associated with longer survival time ($p = 0.037$ and $p = 0.0007$, respectively).²⁶ It is suggested that dietary n-3 fatty acids and arginine may be helpful in these patients.

A diet containing menhaden fish oil may also be used to help reduce inflammatory eicosanoids and metabolic consequences of radiation therapy.⁴¹ It is reported that radiation may lead to accumulation of lactic acid, with inhibition of T cells.⁴² In addition, radiotherapy-induced matrix metalloproteinases may participate in angiogenesis and metastasis of cancer cells.^{43,44} In a randomized double-blind placebo-controlled clinical study, a diet containing menhaden oil resulted in a significantly higher plasma concentration of DHA and EPA in dogs with nasal carcinoma given radiation therapy as compared with control ($p < 0.05$).⁴¹ This diet was also seen to significantly lower tissue inflammatory eicosanoids and decrease resting energy expenditure compared to control. In this study, increased plasma DHA was significantly associated with decreased plasma lactate and matrix metalloproteinases (both $p < 0.05$).⁴¹ It is possible that dietary fish oil may be helpful to lessen negative effects of radiation therapy in dogs with cancer.

Linoleate, a polyunsaturated fatty acid (PUFA) present in safflower oil, may be helpful in some forms of canine cancer.^{45,46} It is reported that linoleic acid may suppress the rate of cell proliferation in human osteogenic sarcoma cells.⁴⁷ In the canine, linoleic acid is converted to γ -linolenic acid, a PUFA that also has a suppressive effect in these cells.^{47,48} In one study, safflower oil containing 76% linoleic acid was seen to produce clinical remission in 6 of 8 dogs with non-responsive mycosis fungoides, a form of canine cutaneous T-cell lymphoma.⁴⁵ In this study, supplementation was associated with an increase in plasma level of non-esterified linoleic acid and was well tolerated by the animals.⁴⁵ In a case study, a supplement containing γ -linolenic acid, linoleic acid, and natural vitamin E was shown to decrease the size of peripheral lymph nodes, spleen, cutaneous nodules, and tonsils in 2 dogs with multicentric lymphoma.⁴⁶ A transient increase in appetite

was seen in both patients. According to Villalobos et al., linoleate at high concentration^b may also be helpful in palliative care of patients with brain neoplasia receiving multimodal therapy.⁴⁹ These findings suggest that linoleate may be beneficial in some cases.

A combination of natural polyphenols may be chemopreventive (i.e. substances that interrupt carcinogenic processes) in canines.⁵⁰ These plant components have demonstrated antioxidant, immune enhancing, and cancer-preventing properties.⁵⁰⁻⁵² It has been reported that the anti-cancer effects of resveratrol may be closely related to its antioxidant properties.⁵³ In a two-phase study, a formulation containing resveratrol, ellagic acid, genistein, curcumin, and quercetin was seen to significantly decrease oxidation of pyrimidine bases caused by hydrogen peroxide in healthy dogs of various breeds as compared to placebo.⁵⁰ The dietary supplement was also shown to alter expression of genes related to oxidative stress. Of interest, measurable serum levels of resveratrol, genistein metabolites, and quercetin (and metabolites) were observed in the treated dogs, and no apparent toxicity was seen. It is suggested that the formula may lessen oxidation of pyrimidine bases in DNA and help in cancer prevention.

A naturally occurring isothiocyanate found in raw cruciferous vegetables, sulforaphane, may be helpful as a chemopreventive and anti-cancer agent.^{54,55} Sulforaphane is released from its precursor glucoraphanin upon damage to the plant.⁵⁴ In a recent study, it was shown that sulforaphane may decrease cell invasion in canine osteosarcoma cell lines.⁵⁵ In the literature, it has been demonstrated that sulforaphane may suppress the growth of tumors and act as an inhibitor of the chromatin-modifying enzyme histone deacetylase (HDAC) in animal models of cancer and in humans.^{54,56} In a study by Curran et al., a single oral dose of a broccoli sprout supplement^c resulted in detectable levels of sulforaphane metabolites in plasma and urine of normal dogs.⁵⁴ In addition, a significant decrease in HDAC activity was seen in peripheral blood mononuclear cells at 24 hours post-consumption. It is reported that sulforaphane may be chemopreventive in part by inhibiting HDACs, which causes reactivation of tumor suppressor genes and eventual cell cycle arrest and apoptosis.⁵⁷ Sulforaphane may be a potentially useful supplement in canine cancer patients.

A sufficient level of vitamin D may lessen the risk of cancer in canines.⁵⁸ A low vitamin D serum level has been associated with an increased risk of various human cancers.⁵⁹ In the literature, it is reported that a low vitamin D serum level may be seen in canine cutaneous mast cell tumor and lymphoma.^{60,61} In some studies, vitamin D metabolites have been shown to have anti-inflammatory and anti-cancer properties.⁶²⁻⁶⁴ In a study by Selting et al., a low 25-hydroxyvitamin D [25(OH)D] serum concentration was seen to be associated with an increased risk of cancer in dogs.⁵⁸ An optimal 25(OH)D serum level was determined to be in the range of 100-120 ng/mL based on the plateauing of various biomarkers at this level. It may be helpful to monitor vitamin D serum level in canine patients with cancer and supplement if needed.⁶⁵

Nutritional Supplements as Supportive Therapy

A supplement containing S-adenosylmethionine (SAME) and silybin-phosphatidylcholine^d may be used to protect the liver in dogs treated with lomustine (CCNU) chemotherapy (Box 1).⁶⁶ S-adenosylmethionine, a molecule formed naturally in the body and found in all living cells, may help in the synthesis of glutathione, an endogenous antioxidant.⁶⁷ Silybin, a flavonolignan in milk thistle (*Silybum marianum*), may conserve glutathione in parenchymal cells.⁶⁸ Its bioavailability is enhanced by phosphatidylcholine, a phospholipid that helps to repair cell membranes. In a prospective randomized study, the SAME and silybin-based supplement combined with CCNU resulted in significantly less elevation in alanine aminotransferase (ALT), aspartate aminotransferase, alkaline phosphatase, and bilirubin in dogs with various malignancies as compared to CCNU alone ($p=0.003$, $p=0.01$, $p=0.009$, and $p=0.02$, respectively).⁶⁶ The combined treatment also showed less decline in serum cholesterol concentration, as a measure of liver function, compared to control ($p=0.02$). In addition, dogs receiving combined therapy were not as likely to experience a delay or discontinuation of treatment due to elevated ALT level. It is suggested that the supplement may be helpful to support the liver in dogs receiving CCNU chemotherapy.

Pyridoxine (vitamin B6) may be helpful to lessen dermatological side effects of chemotherapy.⁶⁹ In patients treated with pegylated liposomal doxorubicin (PLD), a cutaneous reaction known as palmar-plantar erythrodysesthesia (PPES) may be dose limiting. Clinically, PPES is a painful condition that may cause crusting, ulceration, or epidermal necrosis if severe. It is suggested that a natural metabolite of pyridoxine may help in skin barrier repair.^{70,71} In a randomized double-blind placebo-controlled study, oral pyridoxine was seen to significantly decrease the risk of severe PPES and PLD dose reduction in dogs with non-Hodgkin lymphoma receiving PLD^e therapy ($p=0.032$).⁶⁹ In addition, pyridoxine allowed a higher median cumulative dose of PLD compared to control ($p<0.028$). The response to cancer treatment was not impaired by pyridoxine. It was concluded that pyridoxine may be effective in delaying the onset and severity of PPES in canines treated with PLD chemotherapy.

Other natural products that may be helpful in canine cancer include prebiotics and probiotics. It has been demonstrated that probiotics may inhibit tumor progression and modulate the immune response.^{72,73} A polysaccharide of *Cordyceps sinensis* may act as a prebiotic while also enhancing intestinal immunity.⁷⁴ According to Hershey, probiotics may also help to lessen the incidence of diarrhea in patients receiving chemotherapy.⁶⁵ In a small preliminary study, it was shown that a probiotic supplement^f was well tolerated in dogs with multicentric lymphoma undergoing multi-agent chemotherapy.⁷⁵ In this study, dogs receiving the supplement were seen to have fewer episodes of diarrhea compared to placebo, although not statistically significant ($p=0.13$). In a study by Liu et al., it was found that *Dendrobium officinale* combined with American ginseng^g may be used as a prebiotic to enhance short chain

fatty acid (SCFA)-producing genera and prevent gastrointestinal dysbiosis in dogs.⁷⁶ It is possible that prebiotics and probiotics may be helpful supporting supplements. Interestingly, certain cordyceps, dendrobium, and ginseng species (*Dong Chong Xia Cao*, *Shi Hu*, *Xi Yang Shen*, respectively) have been used for centuries as Chinese herbal medicines.⁷⁷⁻⁷⁹

Box 1

Conventional Diets and Supplements Beneficial in Canine Cancer

Diets and Nutritional Supplements

Calorically dense therapeutic diet^{a,30}

Any type of vegetable or yellow-orange vegetables at least 3 times a week³⁴

Chicken, eggs, and coconut/pollack oils ketogenic diet³⁷

Containing menhaden fish oil (n-3 fatty acids) and arginine²⁶

Containing menhaden oil⁴¹

Linoleic acid as safflower oil^{b,45,49}

Formulation containing resveratrol, ellagic acid, genistein, curcumin, and quercetin⁵⁰

Sulforaphane^{c,54}

Vitamin D⁵⁸

Nutritional Supplements as Supportive Therapy

SAME and silybin-phosphatidylcholine complex^{d,66}

Pyridoxine (vitamin B6)⁶⁹

Probiotics^{f,75}

HISTORY OF TRADITIONAL CHINESE MEDICINE TREATMENT IN CANCER

In traditional Chinese medicine (TCM), the earliest records of tumors may be traced to inscriptions on bones and tortoise shells from the Shang Dynasty, in the 16th-11th century BC.^{80,81} In the classic literature, theories and treatments were presented during the Qin Dynasty, in 221-207 BC.⁸⁰ In one of the earliest recorded books on Chinese medicine, the *Huang Di Nei Jing* (The Yellow Emperor's Internal Classic), *Xia-ge* is described as a mass below the diaphragm caused by Blood Stasis.^{81,82} The *Nei Jing* also mentions etiological features, such as inhibited movement of *Ying Qi* or *Wei Qi*, inappropriate joy or anger, improper diet, and unseasonable cold or warmth, that may cause pathogenic factors to accumulate or linger.^{81,83} In *Zhu Bing Yuan Hou Lun* (A General Treatise on the Causes and Symptoms of Diseases), compiled in 610 CE (Common Era or AD), Yuanfang Chao states that Deficiency of the *Zang-fu* organs allows the pathogenic factors to accumulate, eventually resulting in the formation of tumors.^{81,84} In *Yang Ke Xin De Ji* (A Collection of Experiences in the Treatment of Sores), published in 1805 CE, Bingjun Gao adds that Phlegm Stagnation in the *Zang* organs contributes to the pathology of *Ai* or cancer.⁸¹

The early theories of TCM practitioners helped to formulate treatment strategies for cancer.⁸³ In *Zhen Jiu Jia Yi Jing* (The ABC Classic of Acupuncture and Moxibustion), published in 259 CE during the Three Kingdoms period, Mi Huangfu noted the use of acupuncture and moxibustion to treat accumulation of pathogenic factors in the epigastrium.⁸¹ He recommended treatment with acupuncture at CV-13 (*Shang-wan*) if they were located in the upper epigastrium and at CV-10 (*Xia-wan*) if they were located in the lower epigastrium. The indications for using these 2 acupoints include nausea and local pain.^{85,86} In the earliest Chinese materia medica (*Shen Nong Ben Cao Jing*), compiled in the later Han Dynasty (circa 200 CE), herbs used in treating tumors included *Hai Zao* (Sargassum) and *Lian Qiao* (Forsythia).⁷⁷ These herbs are helpful in softening and dissipating masses, respectively.⁷⁸ Some of the Chinese herbal medicine formulas used in ancient times are still in use today, such as *Xiao Jin Dan*, *Xi Huang Wan*, *Da Huang Zhe Chong Wan*, *Liu Shen Wan*, and *Pian Zai Huang*.⁸³

TRADITIONAL CHINESE VETERINARY MEDICINE

Chinese Medical Theory for Cancer

In Chinese medical theory, it is still considered that chronic persistence of pathogenic factors underlies development of cancer.⁸⁷ A weakened *Zheng Qi* (anti-disease capability) is believed to result in susceptibility to extrinsic carcinogenic factors, such as environmental and dietary influences, as well as intrinsic factors, such as congenital deficiencies (i.e. Deficiency of *Jing*).^{3,88} The interaction between a weak body and these factors causes an internal disharmony, leading to a lingering of pathological products such as Phlegm, Damp, and Toxins. The weakened *Zheng Qi* is unable to eliminate these products in a timely manner, causing general pathologic characteristics of cancer: *Qi* Stagnation and Blood Stasis, Phlegm retention, and Toxin accumulation.⁸⁸

In the Chinese medical paradigm, the Stomach *Qi* is the root of all *Qi* in the body.⁸⁷ It is said that illness may be seen as originating from Deficiency of Spleen and Stomach *Qi*. According to the *Pi Wei Lun*, chronic Spleen Deficiency may develop into an environment of Stasis in the Middle *Jiao*, with accumulation of Dampness causing Stasis and Heat.⁸⁹ In this case, there is loss of normalcy in the circulation of *Qi* and Blood and over time a concretion or malignancy may begin to form.^{89,90} If the immune environment is weakened due to malnutrition underlying this condition, and also due to Deficiency of Blood, then it is possible for the malignancy to progress.⁸⁹ It is believed that either brewing of Damp-Heat in Deficiency of Spleen and Stomach *Qi* or effects from external pathogenic factors may give rise to cancer toxins.⁹⁰

As in Chinese herbal medicine (CHM), food therapy is focused on the patient's presenting pattern.³ A Chinese medical diagnosis is made based on *Bian Zheng*, a system of pattern differentiation, using *Si Zhen* (the Four exams).^{91,92} A common Deficiency pattern seen in cancer

patients is Spleen *Qi* Deficiency combined with Blood Deficiency.³ The Excess patterns associated with cancer include Phlegm accumulation, *Qi*-Blood Stagnation, Blood Stasis, and Stagnant Toxic-Heat (Table 1). The principles in cancer therapy were developed from the ancient theories, thus treating the *Yan* or cancer mass while supporting the Spleen and Stomach, is the customary approach used in clinical practice.^{83,87,90} Strategies include strengthening the body's resistance, Heat-clearing and detoxifying, activating Blood to dispel Stasis, and softening/resolving masses.⁸³ As Spleen and Stomach *Qi* Deficiency are considered the root in cancer, it is important to balance the Earth element to support the *Zheng Qi*.³ By nourishing the Spleen *Qi*, the patient is able to produce *Gu Qi* to provide energy and produce Blood. It may also help to reduce or prevent anorexia.^{3,86}

Chinese Herbal Medicine

Polysaccharopeptide (PSP) is a bioactive agent in the mushroom *Coriolus versicolor*, known as *Yun Zhi* in China and used in traditional Chinese medicine for over 2000 years.⁹³ Studies indicate that PSP may suppress tumorigenesis, angiogenesis, and expression of vascular endothelial cell growth factor (VEGF) in animal models.⁹⁴ It may be helpful to delay metastases and improve survival in canine hemangiosarcoma (Box 2).^{93,94} In a double-blind randomized pilot study, high dose PSP was seen to significantly delay metastases in dogs with hemangiosarcoma of the spleen postoperatively as compared to low dose therapy ($p=0.046$).⁹³ The supplement^h, at higher doses, also allowed a longer median survival time than that reported in dogs treated with splenectomy alone. In a recent study, however, the addition of PSP to doxorubicin did not increase survival in dogs with splenic hemangiosarcoma.⁹⁵ It is possible that PSP may have some beneficial effects on survival and quality of life as an alternative therapy.

Yunnan Bai Yao (YBY), a traditional Chinese medicine formula, may lessen hemorrhage and prolong the disease-free interval (DFI) in dogs with hemangiosarcoma.^{78,96,97} *Panax notoginseng* root, *San Qi*, the primary hemostatic herb in YBY, contains ginsenosides that have been shown to inhibit cell proliferation and increase apoptosis in cancer cells.^{78,98} It is reported that YBY may initiate caspase-mediated apoptosis in canine hemangiosarcoma cell lines.⁹⁹ In a study by Ciepluch et al., this herbal medicine formula was seen to prolong the median DFI postoperatively in dogs with splenic hemangiosarcoma, while the administration of blood products and presence of metastatic disease at the time of surgery shortened the DFI ($p=0.01$, $p=0.04$, and $p<0.01$, respectively).⁹⁶ It was found to be relatively safe but did not improve survival in dogs with right atrial mass and pericardial effusion.¹⁰⁰ It is suggested that *Yunnan Bai Yao* may benefit some cases of canine hemangiosarcoma due to the hemostatic as well as anti-cancer properties.

A traditional Chinese herbal medicine, *Wei Chang An* Decoction, may be helpful in canine patients with gastric cancer.¹⁰¹ In China, herbal medicine is widely used in treating advanced gastric cancer in humans.¹⁰² In a non-

clinical randomized controlled study by Han et al., *Wei Chang An* Decoction containing *Tai Zi Shen* (Pseudostellaria), *Bai Zhu* (Atractylodes), *Xia Ku Cao* (Prunella), and other herbs was shown to significantly improve survival time and quality of life in dogs with gastric cancer postoperatively as compared with those receiving either chemotherapy or no treatment following surgery ($p < 0.05$).¹⁰¹ The herbal medicine was also seen to lower the rate of recurrence or metastasis as compared to blank control ($p < 0.05$). The findings suggest that *Wei Chang An* Decoction may be helpful to prevent recurrence or metastasis and improve quality of life in canine postoperative gastric cancer patients.

The Chinese herb *Qing Hao* (Artemisia) may help increase survival time in small animal patients with various types of cancer.¹⁰³ *Qing Hao* has been used to treat fevers and febrile diseases for centuries in traditional Chinese medicine.^{78,104} A main bioactive compound in the herb is the sesquiterpene lactone, artemisinin.^{103,104} It has been reported that Artemisia extract (using *A. annua* species) and artemisinin have anti-cancer effects in canine osteosarcoma cell lines.^{105,106} In a study by Saeed et al., an Artemisia formulationⁱ was shown to significantly improve survival time in canine and feline cancer patients receiving standard therapy as compared to standard therapy alone ($p = 0.0331$).¹⁰³ In addition, the expression level of proliferation marker Ki-67 was associated with artemisinin sensitivity in cancer cells ($p < 0.05$). The use of Artemisia supplementation may improve survival prognosis in small animal cancer patients.

Mammosol^j, a blend of Chinese herbal ingredients, may be helpful to increase survival in canines with mammary cancer.^{107,108} Some of the individual herbs contained in this formula include *Ru Xiang* (Olibanum), *Mo Yao* (Myrrh), and *Huang Qi* (Astragalus). In-vitro studies have shown that Olibanum and Myrrh have anti-breast cancer activities.^{109,110} In a study by Wen et al., Mammosol was seen to significantly increase survival rate in canines with malignant mammary cancer postoperatively as compared with previously published findings in dogs treated with surgery alone and surgery combined with chemotherapy ($p < 0.001$ and $p < 0.05$, respectively).¹⁰⁸ In this study, 7 of the 8 dogs given the supplement lived longer than 2 years and a high quality of life was maintained, as reported by caretakers. It is suggested that Mammosol may be a safe and effective therapy in canine mammary gland cancers.

Chinese Herbal Medicine as Supportive Therapy

Gan Jiang (dry Ginger) may be beneficial in alleviating chemotherapy-induced emesis in canine cancer patients (Box 2). Ginger has been used to treat nausea in traditional Chinese herbal medicine for thousands of years.¹¹¹ In clinical studies, ginger or its active compound, 6-gingerol, has been seen to lessen incidence of nausea and vomiting, increase appetite, and improve quality of life in human cancer patients receiving chemotherapy.^{112,113}

In a study by Sharma et al., the antiemetic efficacy of multidose ginger extracts was assessed in healthy dogs administered an emetic dose of cisplatin.¹¹⁴ It was found that acetone and ethanolic extracts of *Gan Jiang* (dry Ginger) caused a significant decline in mean number of emetic episodes as compared to a cisplatin control (all $p < 0.05$). In some doses, the emetic latency was also seen to increase. The study shows that ginger may be helpful as an antiemetic treatment in cancer chemotherapy.

Lan Zao (Spirulina) is a blue-green microalgae cultivated in China and traditionally used as a food supplement and medical ingredient.^{115,116} A polysaccharide extract of *Spirulina platensis* (PSP) may have beneficial effects on the hematopoietic system in canines given radiation therapy.¹¹⁷ In the literature, there is increasing evidence that the polysaccharides from *Spirulina platensis* may have anti-cancer, antioxidant, and immune enhancing properties.^{115,118,119} In a non-clinical study from China, PSP was seen to significantly increase levels of red cells, white cells, and hemoglobin in the peripheral blood of dogs given ⁶⁰Co- γ irradiation as compared with a model control.¹¹⁷ In addition, PSP was shown to increase the level of granulocytes in the bone marrow compared to control ($p < 0.01$). It was concluded that PSP may be helpful in canines with cancer as an adjunct to radiation therapy.

Sha Chong (Sipunculus) is widely available along the southern coast of China and has been used to clear Heat and balance the Stomach and Spleen in traditional Chinese medicine.¹²⁰⁻¹²² Studies show that the polysaccharide extract of *Sipunculus nudus* (SNP) has antioxidant and immune enhancing activities with a radiation protection effect in dogs.¹²³⁻¹²⁵ In a study by Cui et al., SNP at a moderate dose was seen to significantly improve the recovery level of leukopenia and neutropenia, as well as increase hematopoietic activity in bone marrow in dogs receiving γ -radiation compared to model control ($p < 0.05$).¹²³ The extract of *Sipunculus nudus* also allowed a dose-related increase in superoxide dismutase activity and decrease in nitric oxide serum level compared with control (both $p < 0.05$). In summary, SNP may help to alleviate some of the adverse effects of radiation in canines.

In China, medicinal mushrooms have been used to treat neoplasia and other health conditions for more than 2000 years.^{126,127} These mushrooms contain β -glucan polysaccharides and proteoglycans with immune stimulating and anti-cancer activities.^{72,127} An extract of *Dong Chong Xia Cao* (Cordyceps), a Chinese tonifying herb, has been shown to enhance recovery from leukopenia due to paclitaxel treatment in-vivo.^{128,129} In an open-label trial, a blend of several mushrooms including *Dong Chong Xia Cao* (Cordyceps) and *Yun Zhi* (*Coriolus versicolor*)^k combined with an immunoprotein adjunct^l was seen to lessen the symptoms of neutropenia in dogs with various types of cancer receiving chemotherapy.^{72,130} The combined treatment also helped to maintain quality of life. These findings suggest that mushrooms may be beneficial as a supportive therapy in cancer patients.

Box 2

Chinese Herbal Medicines Beneficial in Canine Cancer

Anti-cancer Activity

Yun Zhi/Coriolus versicolor extract, polysaccharopeptide^h⁹³

*Yunnan Bai Yao*⁹⁶

Wei Chang An Decoction¹⁰¹

*Qing Hao/Artemisia annua*ⁱ¹⁰³

Mammosol^j¹⁰⁸

Supportive Therapy

Gan Jiang/dry Ginger and 6-gingerol¹¹⁴

Lan Zao/Spirulina platensis extract, polysaccharide¹¹⁷

Sha Chong/Sipunculus nudus extract, polysaccharide¹²³

Ba Xi Mo Gu (Brazilian mushrooms/*Agaricus blazei*), *Dong Chong Xia Cao* (Cordyceps/*Cordyceps sinensis* hybrid), *Xiang Xun* (Shiitake mushrooms/*Lentinus edodes*), *Hui Shu Hua* (Maitake mushrooms/*Grifola frondosa*), *Ling Zhi* (Reishi mushrooms/*Ganoderma lucidum*), and *Yun Zhi* (*Coriolus versicolor*) blend^k used with immunoproteins^L¹³⁰

TRADITIONAL CHINESE VETERINARY MEDICINE FOOD THERAPY

In traditional Chinese veterinary medicine (TCVM), the treatment of cancer may combine acupuncture, CHM, *Tui-na*, and food therapy.¹⁰ This approach may be used as a sole therapy or combined with conventional medicine for integrative treatment of these patients. In ancient Chinese texts, it is said that food therapy is helpful in balancing the body. In *Plain Questions: On Soup and Mash*, written more than 2000 years ago, it states that grains boiled for a time and made into mash will nourish the *Zang* organs.¹³¹ A section in *Plain Questions* also describes the distribution of the five flavors of food. Sweet foods are said to benefit the Spleen and may be helpful in cancer patients (e.g. Chinese yam, goji berries, sweet potato). In cases of *Jing* Deficiency, sweet foods may also be helpful to nourish post-natal *Jing*.¹³² Spicy or pungent foods are said to be associated with the Lung and promote the flow of *Qi* and Blood (e.g. chives, watercress, radish).^{3,131} According to Fowler et al., food therapy is helpful in treating the underlying cause and clearing the accumulated Pathogens in cancer patients.³ It may help to slow progression, and in a few cases along with CHM, resolve the disease.

Deficiency Pattern

Spleen *Qi* Deficiency Combined with Blood Deficiency

In this TCVM pattern, a diagnosis is based on signs of *Qi* Deficiency with possible Dryness.³ If the Spleen is Deficient, the *Zheng Qi*, or immune *Qi*, will not be supported well, allowing Pathogens to accumulate. A severe or long-standing *Qi* Deficiency may give rise to Blood Deficiency. This pattern is seen in cancers associated with blood cells or the Spleen, such as mast cell tumors, lymphoma, and hemangiosarcoma. Some clinical signs are lethargy, weakness, and gastrointestinal issues, such as poor appetite and weight loss.^{3,85} The patient

may have dry, dull hair that easily epilates or non-healing sores.³ It is possible to see large flakes of dandruff or dry skin, pads, and nails if Blood Deficiency is prominent. In a TCVM exam, a prominent Spleen *Qi* Deficiency pattern will be evident in the tongue-pulse exam with a pale-wet tongue and deep-weak pulse, particularly on the right.^{3,133} Treatment principles are tonify Spleen *Qi*, nourish Blood in moderation, and prevent Damp and Phlegm accumulation.³

In this case, the aim of food therapy is to support the *Zheng Qi*, balance the Spleen and Stomach, and nourish Blood.³ In some patients, there may be other associated patterns that will need to be treated. In the absence of Cold signs or with concurrent Heat, Damp-Heat, Toxic-Heat, or *Yin* Deficiency, near neutral to cool Spleen *Qi* tonics are used (e.g. sardines, millet, carrots, yams; Table 1). In concurrent global *Qi* Deficiency, *Yang* Deficiency, Cold, or Cold-Damp patterns, warm Spleen *Qi* tonics may be given (e.g. salmon, oatmeal, pumpkin, winter squash). Cardamom and ginger warm the Middle *Jiao* (*Zhong Jiao*) and will benefit the Spleen. A few foods that may help to prevent or treat concurrent Dampness or Phlegm include mackerel, well-cooked pearl barley, lentils, and mushrooms.^{3,87} Foods to nourish Blood include sardines, black beans, blueberries, and fish oil.³ In patients with a weak Spleen, using too many rich Blood tonics may contribute to Dampness. In Spleen *Qi* Deficiency, especially with Damp or Cold signs, it is recommended to avoid raw meats and vegetables, *Yin* or cold foods, and Damp engendering foods, such as dairy, dry processed foods, and saturated fats.^{3,10} In patients with Heat or Stagnant Toxic-Heat, it is suggested to avoid foods with a *Yang* energy.³

Excess Patterns

The Excess patterns of Phlegm accumulation, *Qi*-Blood Stagnation, and Blood Stasis are branches of the Spleen *Qi* Deficiency root and reflect a progression of the disease.^{3,87} In mid- to late-stage cancer patients, Toxic-Heat may develop due to chronic Stagnation.⁸⁷

Phlegm Accumulation

In cancer, substantial Phlegm is considered to be the accumulation of Body Fluid due to a Spleen *Qi* Deficiency.^{3,133} The contributing factors may include a high carbohydrate processed diet, Damp engendering foods, or persistent Damp or Damp-Heat in the environment.^{3,10} In this case, the weakened immune system or *Zheng Qi* is unable to clear the Pathogens, leading to development of soft non-painful masses. Phlegm accumulation is seen in brain tumors, lipomas, thyroid cancer, some skin cancers, and lymphomas.³ A patient may present with lethargy, limb edema or weakness, or other signs of Spleen *Qi* Deficiency.^{3,87} It is also possible to see nausea, vomiting, expectoration of Phlegm, or abdominal distention. In the TCVM exam, the tongue is pale with a greasy coating and may be swollen.^{3,85} The pulse is slippery, possibly reflecting Dampness. Treatment principles are tonify Spleen *Qi*, drain Damp, and transform Phlegm.³

Table 1: Summary of Chinese food therapy to treat common TCVM patterns associated with cancer

| Pattern | Clinical Signs ^{3,10,85,87,133,135,138,139} | Food Therapy ^{3,10,78,87,107,131,132,134-143} |
|---|--|---|
| Deficiency Pattern | | |
| <p>Spleen <i>Qi</i> Deficiency combined with Blood Deficiency</p> | <p>Lethargy, weakness, and gastrointestinal issues, such as poor appetite and weight loss; dry and dull hair that easily epilates, non-healing sores; large flakes of dandruff or dry skin, pads, and nails if Blood Deficiency is prominent</p> <p><u>Tongue:</u> pale, wet</p> <p><u>Pulse:</u> deep and weak, particularly on the right</p> <p><u>Types of cancer:</u> cancers associated with blood cells or the Spleen, such as mast cell tumors, lymphoma, hemangiosarcoma</p> | <p><u>Tonify Spleen <i>Qi</i> and support <i>Zheng Qi</i>:</u></p> <p><u>Near neutral to cool foods:</u> sardines, mackerel, millet, brown rice, Job’s tears, sweet potatoes (red sweet potato is warm), summer squash, carrots, beets, yam, Chinese yam, cabbage, licorice root; use in the absence of Cold signs or with concurrent Heat, Damp-Heat, Toxic-Heat, or <i>Yin</i> Deficiency</p> <p><u>Warm foods:</u> chicken, trout, salmon, oatmeal, sweet rice, pumpkin, winter squash; Chinese ginseng, cardamom, and ginger warm the Middle <i>Jiao</i> (<i>Zhong Jiao</i>); use in concurrent global <i>Qi</i> Deficiency, <i>Yang</i> Deficiency, Cold, or Cold-Damp</p> <p><u>Drain Damp:</u> mackerel, anchovies, well-cooked pearl barley, Job’s tears, lentils, mushrooms, turnip, radish, aduki and red beans, kidney and lima beans, asparagus, celery, pumpkin, blueberries; use to prevent or treat concurrent Dampness or Phlegm</p> <p><u>Nourish Blood:</u> tuna, sardines, egg yolks, dark leafy greens, parsley, beets, carrots, aduki and black beans, kidney and lima beans, apricots, dates, figs, blueberries, blackberries, raspberries, goji berries, longan, fish oil, freshly ground flax seed meal or oil</p> <p>In patients with a weak Spleen, using too many rich Blood tonics may contribute to Dampness</p> <p><u>Foods to avoid especially with Damp or Cold signs:</u> raw meats and vegetables, <i>Yin</i> or cold foods, and Damp engendering foods, such as dairy, dry processed foods, and saturated fats</p> <p>In Heat or Stagnant Toxic-Heat, raw foods may be considered; avoid <i>Yang</i> or hot foods</p> <p>Avoid overuse of high glycemic index foods such as sweet rice</p> |
| Excess Patterns | | |
| <p>Phlegm accumulation</p> | <p>Soft, non-painful masses; lethargy, limb edema or weakness, or other signs of Spleen <i>Qi</i> Deficiency; nausea, vomiting, expectoration of Phlegm, abdominal distention</p> <p><u>Tongue:</u> pale with a greasy coating, may be swollen</p> <p><u>Pulse:</u> slippery, possibly reflecting Dampness</p> <p><u>Types of cancer:</u> brain tumors, lipomas, thyroid cancer, some skin cancers, lymphomas</p> | <p><u>Transform Phlegm:</u> clam, shrimp, mustard greens, radish, oriental radish, winter squash, pumpkin, kelp, seaweed, shiitake or white button mushrooms, wild cabbage, apple, pear, lemon, almonds, walnuts, ginger (<i>Gan Jiang</i>), licorice root, peppermint leaves, thyme, watercress; helpful to include foods to tonify Spleen <i>Qi</i> and drain Damp</p> <p><u>Foods to avoid:</u> cold or raw foods, high carbohydrate processed foods, and Damp engendering foods, such as dairy, peanut butter, and high glycemic index foods</p> |
| <p><i>Qi</i>-Blood Stagnation</p> | <p>A mass that is fixed or variable in size, a purple hue to skin, sharp pain; Blood Stagnation is more painful as compared to <i>Qi</i> Stagnation; irritability</p> <p><u>Tongue:</u> purple</p> <p><u>Pulse:</u> wiry in <i>Qi</i> Stagnation or choppy in Blood Stagnation</p> <p><u>Types of cancer:</u> solid mid-stage tumors</p> | <p><u>Pungent foods:</u> bok choy, broccoli, brussels sprouts, cabbage, collard or mustard greens, kale (slightly bitter-pungent), parsnip, turnip, radish, oriental radish, peaches, peppermint leaves, tangerine peel (<i>Chen Pi</i>), Chinese parsley seed, ginger, turmeric, cumin, watercress, safflower, basil; helpful to include foods to tonify Spleen <i>Qi</i> and nourish Blood</p> <p><u>Sweet foods to move Stagnation:</u> shrimp, sweet rice, eggplant, winter squash, strawberry, Hawthorn berry, plum, cherry, chestnut, rice vinegar in small amounts</p> <p><u>Circulate <i>Qi</i>:</u> carrots, cabbage, mustard greens, radish, crabapple, lychee, lemon, plum, mango, Mandarin orange and tangerine peel, Chinese parsley seed, cinnamon, ginger, licorice root, turmeric, thyme, basil</p> <p><u>Circulate Blood:</u> crab, sturgeon, mussel, mustard greens, kale, eggplant, winter squash, peaches, Hawthorn berry, chestnuts, citrus peel, turmeric, safflower, and apple cider, Chinese fermented, or rice vinegar in small amounts</p> <p><u>Foods to avoid:</u> Stagnation promoting foods, such as refined carbohydrates, starchy treats, excess fats and dairy, overall thermally hot diets, and glutens, as they may be pro-inflammatory</p> |

Table 1: Cont

| Pattern | Clinical Signs ^{3,10,85,87,133,135,138,139} | Food Therapy ^{3,10,78,87,107,131,132,134-143} |
|---------------------|--|---|
| Blood Stasis | <p>Fixed, irregularly shaped masses that are very painful, masses that are painful especially when palpated, a purple hue to skin, bleeding; insomnia</p> <p><u>Tongue</u>: purple, may have prominent veins</p> <p><u>Pulse</u>: choppy</p> <p><u>Types of cancer</u>: solid late-stage tumors, such as liver or bladder cancer</p> | <p><u>Break up and move Stagnation</u>: shrimp, crab, collard or mustard greens, kale, radish, peaches, Hawthorn berry, crabapple, tangerine peel, turmeric, and apple cider, Chinese fermented, or rice vinegar in small amounts; helpful to include pungent foods as well as foods to specifically circulate Blood and nourish Blood</p> <p><u>Foods to avoid</u>: overly hot or cold diets and stagnating foods, such as highly processed dry foods, fatty foods, and dairy</p> |
| Stagnant Toxic-Heat | <p>Locally destructive cancerous masses, pain, inflammation or infection in and around a mass, foul discharges, tumor necrosis; possible fever, redness, cool-seeking behavior; irritability</p> <p><u>Dry and Heat signs</u>: thirst, concentrated urine, constipation</p> <p><u>Tongue</u>: dark red or purple with a yellow coating</p> <p><u>Pulse</u>: fast, full, bounding or choppy</p> <p><u>Types of cancer</u>: late-stage or aggressive tumors; osteosarcoma, fibrosarcoma, transitional cell tumor of the bladder, advanced mammary cancer</p> | <p><u>Clear Heat and tonify Yin</u>: clam, crab, scallop, deep ocean whitefish, chicken egg white, tofu, amaranth, millet, Job's tears, brown rice, broccoli, bamboo leaf or sprout, dandelion or mulberry leaf, lotus leaf, kelp, seaweed, spinach, celery, cucumber, bitter melon, eggplant, zucchini, green or string bean, mung bean or sprout, white button or Enokitake mushroom, lemon, pear, mango, blueberry, banana, black sesame seed, flax seed, green algae, chrysanthemum flower, peppermint leaf, soybean oil; helpful to include foods to tonify Qi, nourish Blood, and resolve Stagnation, avoiding items with a Yang or hot energy</p> <p>Omega-3 fatty acids found in fish oil and krill oil are Yin and Blood tonics and may be used as tolerated by the Spleen</p> <p><u>Detoxify</u>: clam, tofu, amaranth, dandelion, spinach, water spinach, bok choy, rhubarb, Swiss chard, sweet potato, carrot, radish, turnip, beet, black or aduki bean, mung bean or sprout, green peas, blueberry, Chinese plum, pitaya, water chestnut, fig, microalgae, green algae, licorice root, basil, parsley, wintergreen, honey, sesame oil, and apple cider, rice, or Chinese fermented vinegar in small amounts</p> <p><u>Foods to avoid</u>: hot or very warm foods, herbs, and spices and stagnating foods, such as dairy, fatty foods, high carbohydrate processed foods, and starchy treats</p> |

In this pattern, it is helpful to include foods to tonify the Spleen and drain Damp, along with pungent foods to transform Phlegm.³ Some pungent foods to transform Phlegm include mustard greens, oriental radish, wild cabbage, and *Gan Jiang* (dry Ginger), (Table 1).^{3,134} Foods that serve as both culinary products and herbal medicines to transform Phlegm include *Bo He* (peppermint leaves), *Bai Li Xiang* (thyme), and *Xi Yang Cai* (watercress).³ It is recommended to avoid cold or raw foods, high carbohydrate processed foods, and Damp engendering foods, such as dairy, peanut butter, and high glycemic index foods.

Qi-Blood Stagnation

In persistent Phlegm accumulation, the free flow of Qi and Blood is impeded, leading to Stagnation and development of solid mid-stage tumors.^{3,87} Some other causes of Qi and Blood Stagnation are lingering external Pathogens such as Cold and Damp, trauma/injuries, and emotional imbalance affecting the flow of Liver Qi. Clinical signs in cancer patients may include a mass that is fixed or variable in size, a purple hue to skin, and sharp pain. The patient may also have irritability. In the exam, the tongue may be purple. The pulse is wiry in Qi Stagnation or choppy in Blood Stagnation. The treatment principles are promote the circulation of Qi and Blood, resolve Stagnation, and tonify Qi and Blood as needed.^{3,135}

If Qi-Blood Stagnation is present, the intent is to move Stagnation using pungent foods and nourish Qi and Blood.³ While pungent foods have varying thermal properties, they promote the circulation of Qi and Blood and are helpful to relieve pain. Pungent foods and herbs may also have anti-cancer properties and prevent post-radiation fibrosis.^{3,107} A few pungent foods are cabbage, collard greens, kale, and *Chen Pi* (tangerine peel), (Table 1).^{3,136} Some foods with a sweet taste that move Stagnation may be given (e.g. shrimp, Hawthorn berry, strawberry, and rice vinegar in small amounts). Foods to specifically circulate Qi include carrots, crabapple, cinnamon, and licorice root.^{3,137} Foods to circulate Blood include crab, kale, winter squash, and chestnut. It is recommended to avoid Stagnation promoting foods (e.g. refined carbohydrates, starchy treats, excess fats, dairy), overall thermally hot diets, and glutens (may be pro-inflammatory).³

Blood Stasis

Blood Stasis is considered an end stage of Qi-Blood Stagnation in cancer patients.³ In this pattern, the flow of Blood is completely blocked, leading to the development of fixed, irregularly shaped masses that are very painful. As Qi is needed to move Blood, a Deficiency of Qi or Stagnation of Qi may cause the Blood to stagnate and eventually result in Blood Stasis. Interior Cold, as well as Heat in the Blood may also cause Stasis.^{85,87} This pattern is seen in solid late-stage tumors, such as liver or bladder

cancer.^{3,87} Clinical signs include masses that are painful, especially when palpated, a purple hue to skin, bleeding, and sometimes insomnia. In the exam, the tongue is purple, may have prominent veins, and pulses can be choppy. The treatment principles are break up Stasis and nourish Blood.³

In Blood Stasis, the aim is to supplement with pungent foods to break up Stagnation and circulate Blood combined with foods to nourish Blood.³ A few foods to break up and move Stagnation include shrimp, collard/mustard greens, peaches, and the herb *Jiang Huang* (turmeric), (Table 1). Some of the cruciferous vegetables are pungent and may be especially helpful in patients with cancer. A supplement containing turmeric and black pepper referred to as Golden Paste may also be beneficial (Table 2).^{3,138} Research indicates that this combination may have a stronger anti-cancer effect than either ingredient alone.³ It is recommended to avoid overly hot or cold diets and stagnating foods, such as highly processed dry foods, fatty foods, and dairy.

Table 2: Golden Paste recipe for dogs

| Ingredient | Amount |
|---|-------------|
| Organic powdered turmeric | ½ cup |
| Filtered water | 1 to 1½ cup |
| Ethically sourced, organic coconut oil | ¼ to ½ cup |
| Freshly ground black pepper | ½ to 1½ tsp |
| <p>Add turmeric to water in a pan on low heat and stir for 7 to 10 minutes until thickened. Turn off heat and stir in black pepper and oil, allowing mixture to cool. Store in refrigerator and use within 2 weeks.</p> <ul style="list-style-type: none"> - Small dogs should start with about ¼ tsp per day - Medium dogs can start with ¼ tsp per day - Large dogs can start with ½ tsp per day - Giant dogs can start with ¾ tsp per day <p>It is recommended to work up to ¼ to ½ tsp per day for every 10 lbs of weight (½ to 1 tsp for a 40 lb dog). There is controversy regarding the use of golden paste in cats.</p> <p>tsp=teaspoon</p> | |

Adapted from: Alinovi C. *Materia medica – frequently used foods for TCVM food therapy. Integrative and Traditional Chinese Veterinary Medicine Food Therapy: Small Animal and Equine.* Fowler M, Xie H (eds). Reddick, FL: Chi University Press 2020:166.³

Stagnant Toxic-Heat

In some late-stage cancers, Blood Stasis may progress to Stagnant Toxic-Heat.³ A patient may also develop internal Heat or Fire by consuming *Yang* or dry high carbohydrate processed foods or as a consequence of Heat invading from the environment.^{3,87} Stagnant Toxic-Heat may be seen in aggressive or locally destructive tumors, including osteosarcoma, fibrosarcoma, transitional cell tumor of the bladder, and advanced mammary cancer. Some clinical signs of Heat or inflammation are fever, redness, infection in and around a tumor, and cool-seeking behavior.^{3,139} Dry and Heat signs may include thirst, concentrated urine, and constipation. It is also possible to see irritability. In the exam, the tongue may be dark red or purple with a yellow coating.³ The pulse is fast, full, and

bounding or choppy. Treatment principles are tonify *Yin*, nourish *Qi* and Blood, clear Heat, and detoxify.

If Stagnant Toxic-Heat is present, foods that clear Heat, tonify *Yin*, and detoxify are given.³ In research studies, herbal medicine and foods that clear Heat have been shown to have anti-cancer, anti-inflammatory, and immune enhancing properties.¹⁴⁴⁻¹⁴⁶ A few foods to clear Heat and tonify *Yin* include scallop, seaweed, blueberry, and peppermint leaf (Table 1).³ Some foods to clear Toxins are clam, carrot, Chinese plum, and wintergreen. Additionally, as the root is *Qi* Deficiency, it is helpful to use foods to tonify *Qi* and nourish Blood according to the presenting pattern.^{3,140} Foods to resolve Stagnation may also be used, avoiding items with a *Yang* energy.³ It is suggested to avoid hot or very warm foods, herbs, spices and stagnating foods, such as dairy, fatty foods, high carbohydrate processed foods, and starchy treats.

CONSIDERATIONS – HUMAN LITERATURE

In humans, certain dietary patterns may help lessen risk or improve long-term survival in some types of cancer. It is suggested in the literature that a diet containing fruits and vegetables, nuts, whole grains, fish, omega-3 fatty acids, soy, and probiotics may be beneficial.¹⁴⁷⁻¹⁵² A case-control study conducted in Connecticut found that a pre-diagnostic high intake of vegetables and citrus fruits appeared to prolong survival in patients with non-Hodgkin lymphoma.¹⁵³ In particular, a high intake of green leafy vegetables and cruciferous vegetables favored survival in patients with T-cell lymphoma. In another study, fish oil was shown to have a beneficial effect on long-term survival in patients with hematological malignancies receiving chemotherapy.¹⁵⁴ Fish oil was also seen to lessen C-reactive protein serum level as compared to non-supplemented control, indicating a decrease in risk of inflammation. In some studies, red and processed meat, saturated fatty acids, and a high glycemic diet were positively related with cancer.^{147,155} As the pathology may be similar in some canine and human cancers, the findings in these studies are consistent with the idea that dietary patterns may be helpful in lessening risk and improving survival in dogs.^{156,157}

It is possible that diet may help in preventing or treating cancer by influencing the intestinal microbiome. In a study by Zamani et al., *Lactobacillus acidophilus* intake was seen to significantly increase the serum level of CYLD protein in patients with rectal cancer as compared with placebo control, leading to an anti-inflammatory effect.¹⁵² In this study, *L. acidophilus* was also found to improve survival compared to control ($p < 0.05$). In the literature, it is reported that bacterial fermentation of dietary fiber produces short chain fatty acids such as butyrate that may benefit patients with colorectal cancer.^{158,159} Short chain fatty acids may cause a decrease in pro-inflammatory cytokines and lessen the proliferation of cancer cells.^{159,160} In clinical trials, dietary almonds and walnuts were seen to increase SCFA-producing bacteria in the intestinal microbiome and may help in preventing colorectal cancer in humans.¹⁴⁸

From a Chinese medical viewpoint, food therapy is given to maintain a balance in the body, prevent or treat illness, and slow aging.¹³¹ In China, there is a long history of treating masses and their associated patterns using specific foods or medicinal herbs.^{77,81} In the *Shen Nong Ben Cao Jing*, it is said that *Hai Zao* (seaweed) is cold and bitter, breaks and disperses bound *Qi*, and helps in treating tumors and nodes in the neck.⁷⁷ In clinical practice, foods such as seaweed, shiitake mushroom, loquat fruit, and pear are given to transform Phlegm, benefit the throat, and soften hardness and may be used in canine lymph node cancers.^{81,87} *Shen Nong* also mentions *Da Zao* (Chinese date), *Ying Tao* (cherry), and *Hu Ma* (sesame seed) as foods with a sweet flavor that nourish the Spleen and *Qi*.⁷⁷ It is said that long-term intake of Chinese date and sesame seed may lengthen life. In recent literature, it is mentioned that the Chinese date contains triterpenic acids, which have a variety of activities such as anti-inflammatory and anti-cancer effects.^{161,162}

INTEGRATIVE NUTRITION

There is evidence in the literature that dietary therapy is helpful in canine cancer.^{3,72} It is possible, with consideration of human literature both ancient and modern, that a combination of syndrome differentiation in Chinese food therapy (CFT) and conventional nutritional therapy

may be used to treat canine cancer patients. A Chinese paper reported that an increased efficacy was seen when CFT was combined with conventional nutritional therapy in humans.¹⁶³ As an example, a study by Shen et al. found that foods with a cold nature and high in potassium, magnesium, calcium, and fiber were more effective in treating hypertension in patients with *Yin* Deficiency.^{163,164} It is important to remember that most cases of cancer involve one or more of the main Deficiency syndromes (e.g. *Yin*, *Yang*, *Qi*, Blood), as well as Stagnation or the more severe form, Stasis.^{3,139} Using CFT in dogs, near neutral to cool foods are recommended in cases of Spleen *Qi* Deficiency combined with Blood Deficiency with concurrent *Yin* Deficiency, and adding fresh coriander seed, thyme, or turmeric (<1% of diet) helps to relieve Stagnation.³ Vinegar is used to break up Stasis, soothe Liver *Qi*, aid digestion and is anti-cancer when used in small amounts.

With consideration of the *Bian Zheng* or TCVM pattern diagnosis, conventional supplements that have demonstrated efficacy, such as SAME-silybin^d and fish oil, may be added to a Chinese food therapy diet.³ Chinese and Western herbal medicine may also be added to the diet, if accepted by the patient. Clients are more likely to consider dietary therapy, especially with its variety of options, than other cancer treatments, making it a useful therapy that may benefit survival and quality of life in canine patients (Integrative Diet example, Table 3).

Table 3: Integrative oncology diet for a patient with Spleen *Qi* Deficiency, Phlegm accumulation, and Blood Stagnation

| Ingredient | Daily Amount |
|--|--|
| <i>Select 1:</i> Chicken thigh, boneless, skinless, roasted (alternating) Turkey, ground, 93% lean, pan-browned Atlantic cod filet, boneless, skinless, baked | 135 g cooked 110 g cooked 140 g cooked |
| <i>Select 1:</i> Wild rice, cooked, without salt Amaranth, cooked, without salt Sweet potato, baked, skin discarded, mashed | 100 g cooked 100 g cooked 110 g cooked |
| <i>Select 2*:</i> Kale Spinach Green beans Broccoli Carrots Cucumber with peel Celery Asparagus Cauliflower Blueberries Apple with skin Steam or boil the vegetables until soft. The fruit, carrots, celery, and cucumber may be left raw if desired and finely chopped or pulverized. | 40 g raw 85 g raw 65 g raw 60 g raw 50 g raw 125 g raw 125 g raw 95 g raw 80 g raw 35 g raw 40 g raw |
| Flaxseed oil, cold pressed | 2¼ tsp with cod only |
| Veterinarian Recommended Solutions Omega Benefits Canine | 1 pump (3 mL) |
| Chicken egg, hard boiled, shell discarded | 1 large (50 g) |

Table 3: Cont

| Ingredient | Daily Amount |
|--|---------------|
| Balance IT Canine | 3 tsp (7.5 g) |
| Herbs, optional: up to 1 tsp total per meal of one or a combination of the following, fresh: ginger, turmeric, parsley, thyme, clove, coriander, dill seed Mix all ingredients together thoroughly Approximately 480 kcal per day *each fruit and vegetable option is approximately 20 kcal Nutrient Analysis with kale and blueberries: 33.2-38.3% Metabolizable Energy (ME) protein, 37.3-42.8% ME fat, 22.5-26.2% ME carbohydrate; 2.6-2.7 g calcium per 1000 kcal, 2.0-2.4 g phosphorus per 1000 kcal, 3.1-4.0 g potassium per 1000 kcal, 0.5-0.7 g sodium per 1000 kcal; <i>recipe meets AAFCO 2016 dog food nutrient profiles for adult maintenance</i> g=gram; tsp=teaspoon; mL=milliliter | |

Adapted from: Fowler M, Pope K. Food therapy for cancer. Integrative and Traditional Chinese Veterinary Medicine Food Therapy: Small Animal and Equine. Fowler M, Xie H (eds). Reddick, FL: Chi University Press 2020:505-506.³

SUMMARY

In humans and animals, it has been demonstrated in the literature that diet is an important aspect of cancer prevention and treatment. A diet or supplements rich in nutrients that support immunity and lessen cell invasion such as polyphenols and sulforaphane may intervene in pathological processes related to cancer in dogs. Traditional Chinese medicine has been applied in cancer patients for centuries and may be integrated with conventional nutritional therapy or used as a sole treatment. Chinese food therapy is based on *Bian Zheng* or diagnosis of a disease pattern of imbalance. A selection of foods is then used to create a balanced diet addressing the unique pattern observed in a patient. Integrative dietary therapy offers clinicians a personalized treatment in cancer to help improve survival and quality of life.

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FOOTNOTES

- ^a Hill's Prescription Diet ONC Care Canine dry, Hill's Pet Nutrition, Inc., Topeka, Kansas, USA
- ^b eSutras linoleic acid, TC Bauer Co., Chicago, Illinois, USA
- ^c BroccoMax, Jarrow Formulas, Los Angeles, California, USA
- ^d Denamarin, Nutramax Laboratories, Inc., Edgewood, Maryland, USA
- ^e Doxil, Sequus Pharmaceuticals, Menlo Park, California, USA
- ^f Visbiome, ExeGi Pharma, LLC, Rockville, Maryland, USA
- ^g Tiepi Fengdoujing (TPFDJ), Hangzhou Huqing Yutang Pharmaceutical Co., Ltd., China
- ^h I'm-Yunity, Integrated Chinese Medicine Holdings, Ltd., Hong Kong, China
- ⁱ Luparte, Lupovet GmbH Veterinary Diets, Müllheim, Germany
- ^j Mammosol, Natural Solutions, Inc., Speonk, New York, USA
- ^k K-9 Immunity, Aloha Medicinals, Inc., Carson City, Nevada, USA
- ^L K-9 Transfer Factor, Aloha Medicinals, Inc., Carson City, Nevada, USA

REFERENCES

1. Yu C, Song G, Yhee J et al. Histopathological and immunohistochemical comparison of the brain of human patients with Alzheimer's disease and the brain of aged dogs with cognitive dysfunction. *J Comp Pathol* 2011; 145(1):45-58. <https://doi.org/10.1016/j.jcpa.2010.11.004>
2. Sarver A, Makielski K, DePauw T et al. Increased risk of cancer in dogs and humans: A consequence of recent extension of lifespan beyond evolutionarily determined limitations? *Aging Cancer* 2022; 3(1):3-19. <https://doi.org/10.1002/aac2.12046>
3. Fowler M, Xie H. Integrative and Traditional Chinese Veterinary Medicine Food Therapy: Small Animal and Equine. Reddick, FL: Chi University Press 2020:483-529, 21-177, 719-848.
4. Smith N, Luethcke K, Craun K et al. Risk of bladder cancer and lymphoma in dogs is associated with pollution indices by county of residence. *Vet Comp Oncol* 2022; 20(1):246-255. <https://doi.org/10.1111/vco.12771>
5. Baek S, McEntee M, Legendre A. Review paper: Cancer chemopreventive compounds and canine cancer. *Vet Pathol* 2009; 46(4):576-588. <https://doi.org/10.1354/vp.08-VP-0238-B-REV>
6. Saba C. Vaccine-associated feline sarcoma: current perspectives. *Vet Med (Auckl)* 2017; 8:13-20. <https://doi.org/10.2147/VMRR.S116556>
7. Hart L, Thigpen A, Hart B et al. Assisting decision-making on age of neutering for German Short/Wirehaired Pointer, Mastiff, Newfoundland, Rhodesian Ridgeback, Siberian Husky: associated joint disorders, cancers, and urinary incontinence. *Front Vet Sci* 2024; 11:1322276. <https://doi.org/10.3389/fvets.2024.1322276>
8. Hastings P, Lupski J, Rosenberg S et al. Mechanisms of change in gene copy number. *Nat Rev Genet* 2009; 10(8):551-564. <https://doi.org/10.1038/nrg2593>
9. Xavier P, Müller S, Fukumasu H. Epigenetic mechanisms in canine cancer. *Front Oncol* 2020; 10:591843. <https://doi.org/10.3389/fonc.2020.591843>
10. Yamate M. TCVM: An integrative approach to treating cancer. *IVC Journal* 2019; 9(2):54-58. <https://ivcjournal.com/tcvm-an-integrative-approach-to-treating-cancer/>
11. Chavalle T, Chamel G, Denoeux P et al. Are severe adverse events commonly observed in dogs during cancer chemotherapy? A retrospective study on 155 dogs. *Vet Comp Oncol* 2022; 20(2):393-403. <https://doi.org/10.1111/vco.12782>
12. Blackwood L, Tanis J, Harper A et al. Acute radiotherapy toxicity in 57 dogs with gross and microscopic mast cell tumours. *Vet Comp Oncol* 2018; 16(4):431-440. <https://doi.org/10.1111/vco.12398>
13. Marconato L, Aresu L, Stefanello D et al. Opportunities and challenges of active immunotherapy in dogs with B-cell lymphoma: a 5-year experience in two veterinary oncology centers. *J Immunother Cancer* 2019; 7(1):146. <https://doi.org/10.1186/s40425-019-0624-y>
14. Zandvliet M, Teske E. Mechanisms of drug resistance in veterinary oncology- a review with an emphasis on canine lymphoma. *Vet Sci* 2015; 2(3):150-184. <https://doi.org/10.3390/vetsci2030150>
15. Koshino A, Goto-Koshino Y, Setoguchi A et al. Mutation of p53 gene and its correlation with the clinical outcome in dogs with lymphoma. *J Vet Intern Med* 2016; 30(1):223-229. <https://doi.org/10.1111/jvim.13807>

16. Dressler D. Integrated approaches to canine cancer: Augmentative treatment strategies. *IVC Journal* 2019; 9(3):10-13. <https://ivcjournal.com/integrated-approaches-canine-cancer-treatment/>
17. Biller B, Guth A, Burton J et al. Decreased ratio of CD8+ T cells to regulatory T cells associated with decreased survival in dogs with osteosarcoma. *J Vet Intern Med* 2010; 24(5):1118-1123. <https://doi.org/10.1111/j.1939-1676.2010.0557.x>
18. Alonso-Miguel D, Valdivia G, Guerrero D et al. Neoadjuvant in situ vaccination with cowpea mosaic virus as a novel therapy against canine inflammatory mammary cancer. *J Immunother Cancer* 2022; 10(3):e004044. <https://doi.org/10.1136/jitc-2021-004044>
19. Doyle H, Gee R, Masters T et al. Vaccine-induced ErbB (EGFR/HER2)-specific immunity in spontaneous canine cancer. *Transl Oncol* 2021; 14(11):101205. <https://doi.org/10.1016/j.tranon.2021.101205>
20. Zollers B, Rhodes L, Smith R. Capromorelin increases food consumption, body weight, growth hormone, and sustained insulin-like growth factor 1 concentrations when administered to healthy adult Beagle dogs. *J Vet Pharmacol Ther* 2017; 40(2):140-147. <https://doi.org/10.1111/jvp.12344>
21. Zollers B, Wofford J, Heinen E et al. A prospective, randomized, masked, placebo-controlled clinical study of capromorelin in dogs with reduced appetite. *J Vet Intern Med* 2016; 30(6):1851-1857. <https://doi.org/10.1111/jvim.14607>
22. Johannes C. The evolving clinical management of chronic inappetence. *Today's Veterinary Practice* 2023; 13(2):22-26. <https://todaysveterinarypractice.com/nutrition/the-evolving-clinical-management-of-chronic-inappetence/>
23. Rhodes L, Zollers B, Wofford J et al. Capromorelin: a ghrelin receptor agonist and novel therapy for stimulation of appetite in dogs. *Vet Med Sci* 2017; 4(1):3-16. <https://doi.org/10.1002/vms3.83>
24. Guy M, Teixeira A, Shrier A et al. Effects of orally administered crofelemer on the incidence and severity of neratinib-induced diarrhea in female dogs. *PLoS One* 2024; 19(1):e0282769. <https://doi.org/10.1371/journal.pone.0282769>
25. Budde J, McCluskey D. Plumb's Veterinary Drug Handbook 10th Ed. Hoboken, NJ: Wiley-Blackwell 2023:316, 317.
26. Ogilvie G, Fettman M, Mallinckrodt C et al. Effect of fish oil, arginine, and doxorubicin chemotherapy on remission and survival time for dogs with lymphoma: a double-blind, randomized placebo-controlled study. *Cancer* 2000; 88(8):1916-1928. [https://doi.org/10.1002/\(SICI\)1097-0142\(20000415\)88:8<1916::AID-CNCR22>3.0.CO;2-F](https://doi.org/10.1002/(SICI)1097-0142(20000415)88:8<1916::AID-CNCR22>3.0.CO;2-F)
27. Lei Y, Ho S, Kwok C et al. Association of high adherence to vegetables and fruits dietary pattern with quality of life among Chinese women with early-stage breast cancer. *Qual Life Res* 2022; 31(5):1371-1384. <https://doi.org/10.1007/s11136-021-02985-0>
28. Song M, Zhang X, Meyerhardt J et al. Marine ω-3 polyunsaturated fatty acid intake and survival after colorectal cancer diagnosis. *Gut* 2017; 66(10):1790-1796. <https://doi.org/10.1136/gutjnl-2016-311990>
29. Block K, Block P, Gyllenhaal C. Integrative treatment for colorectal cancer: a comprehensive approach. *J Altern Complement Med* 2018; 24(9-10):890-901. <https://doi.org/10.1089/acm.2018.0125>
30. Anthony R, Amundson M, Brejda J et al. Acceptance of a novel, highly palatable, calorically dense, and nutritionally complete diet in dogs with benign and malignant tumors. *Vet Sci* 2023; 10(2):148. <https://doi.org/10.3390/vetsci10020148>
31. Michel K, Sorenmo K, Shofer F. Evaluation of body condition and weight loss in dogs presented to a veterinary oncology service. *J Vet Intern Med* 2004; 18(5):692-695. [https://doi.org/10.1892/0891-6640\(2004\)18<692:eobcaw>2.0.co;2](https://doi.org/10.1892/0891-6640(2004)18<692:eobcaw>2.0.co;2)
32. Romano F, Heinze C, Barber L et al. Association between body condition score and cancer prognosis in dogs with lymphoma and osteosarcoma. *J Vet Intern Med* 2016; 30(4):1179-1186. <https://doi.org/10.1111/jvim.13965>
33. Lee W, Lee J, Liao A et al. Association between weight change during initial chemotherapy and clinical outcome in dogs with multicentric lymphoma. *Vet Comp Oncol* 2021; 19(1):53-60. <https://doi.org/10.1111/vco.12637>
34. Raghavan M, Knapp D, Bonney P et al. Evaluation of the effect of dietary vegetable consumption on reducing risk of transitional cell carcinoma of the urinary bladder in Scottish Terriers. *J Am Vet Med Assoc* 2005; 227(1):94-100. <https://doi.org/10.2460/javma.2005.227.94>
35. Wu S, Liu Y, Michalek J et al. Carotenoid Intake and circulating carotenoids are inversely associated with the risk of bladder cancer: a dose-response meta-analysis. *Adv Nutr* 2020; 11(3):630-643. <https://doi.org/10.1093/advances/nmz120>
36. Tang J, Wang R, Zhong H et al. Vitamin A and risk of bladder cancer: a meta-analysis of epidemiological studies. *World J Surg Oncol* 2014; 12:130. <https://doi.org/10.1186/1477-7819-12-130>
37. Seyfried T, Mukherjee P, Lee D et al. Case report: Resolution of malignant canine mast cell tumor using ketogenic metabolic therapy alone. *Front Nutr* 2023; 10:1157517. <https://doi.org/10.3389/fnut.2023.1157517>
38. Winter S, Loebel F, Dietrich J. Role of ketogenic metabolic therapy in malignant glioma: A systematic review. *Crit Rev Oncol Hematol* 2017; 112:41-58. <https://doi.org/10.1016/j.critrevonc.2017.02.016>
39. Mandal C, Ghosh-Choudhury T, Yoneda T et al. Fish oil prevents breast cancer cell metastasis to bone. *Biochem Biophys Res Commun* 2010; 402(4):602-607. <https://doi.org/10.1016/j.bbrc.2010.10.063>
40. Kirk S, Hurson M, Regan M et al. Arginine stimulates wound healing and immune function in elderly human beings. *Surgery* 1993; 114(2):155-160.
41. Hansen R, Anderson C, Fettman M et al. Menhaden oil administration to dogs treated with radiation for nasal tumors demonstrates lower levels of tissue eicosanoids. *Nutr Res* 2011; 31(12):929-936. <https://doi.org/10.1016/j.nutres.2011.09.018>
42. Tang L, Wei F, Wu Y et al. Role of metabolism in cancer cell radioresistance and radiosensitization methods. *J Exp Clin Cancer Res* 2018; 37(1):87. <https://doi.org/10.1186/s13046-018-0758-7>
43. Artacho-Cordón F, Ríos-Arrabal S, Lara P et al. Matrix metalloproteinases: potential therapy to prevent the development of second malignancies after breast radiotherapy. *Surg Oncol* 2012; 21(3):e143-e151. <https://doi.org/10.1016/j.suronc.2012.06.001>
44. Merchant N, Nagaraju G, Rajitha B et al. Matrix metalloproteinases: their functional role in lung cancer. *Carcinogenesis* 2017; 38(8):766-780. <https://doi.org/10.1093/carcin/bgx063>
45. Iwamoto K, Bennett L, Norman A et al. Linoleate produces remission in canine mycosis fungoides. *Cancer Lett* 1992; 64(1):17-22. [https://doi.org/10.1016/0304-3835\(92\)90016-o](https://doi.org/10.1016/0304-3835(92)90016-o)
46. Williams J. The use of gamma linolenic acid, linoleic acid and natural vitamin E for the treatment of multicentric lymphoma in two dogs. *J S Afr Vet Assoc* 1988; 59(3):141-144.
47. Booyens J, Engelbrecht P, le Roux S et al. Some effects of the essential fatty acids linoleic acid and alpha-linolenic acid and of their metabolites gamma-linolenic acid, arachidonic acid, eicosapentaenoic acid, docosahexaenoic acid, and of prostaglandins A1 and E1 on the proliferation of human osteogenic sarcoma cells in culture. *Prostaglandins Leukot Med* 1984; 15(1):15-33. [https://doi.org/10.1016/0262-1746\(84\)90053-2](https://doi.org/10.1016/0262-1746(84)90053-2)
48. Crisi P, Luciani A, Di Tommaso M et al. The fatty acid-based erythrocyte membrane lipidome in dogs with chronic enteropathy. *Animals (Basel)* 2021; 11(9):2604. <https://doi.org/10.3390/ani11092604>
49. Villalobos A, Hershey B. *Cancers in dogs and cats. Hospice and Palliative Care for Companion Animals: Principles and Practice* 2nd Ed. Shanahan A, Pierce J, Shearer T (eds). Hoboken, NJ: Wiley-Blackwell 2023:121-137.
50. Kondratyuk T, Adrian J, Wright B et al. Evidence supporting the conceptual framework of cancer chemoprevention in canines. *Sci Rep* 2016; 6:26500. <https://doi.org/10.1038/srep26500>
51. Izuogbuna O. Polyphenols: Chemoprevention and therapeutic potentials in hematological malignancies. *Front Nutr* 2022; 9:1008893. <https://doi.org/10.3389/fnut.2022.1008893>
52. Niedzwiecki A, Roomi M, Kalinovsky T et al. Anticancer efficacy of polyphenols and their combinations. *Nutrients* 2016; 8(9):552. <https://doi.org/10.3390/nu8090552>
53. Athar M, Back J, Tang X et al. Resveratrol: a review of preclinical studies for human cancer prevention. *Toxicol Appl Pharmacol* 2007; 224(3):274-283. <https://doi.org/10.1016/j.taap.2006.12.025>
54. Curran K, Bracha S, Wong C et al. Sulforaphane absorption and histone deacetylase activity following single dosing of broccoli sprout supplement in normal dogs. *Vet Med Sci* 2018; 4(4):357-363. <https://doi.org/10.1002/vms3.118>

55. Rizzo V, Levine C, Wakshlag J. The effects of sulforaphane on canine osteosarcoma proliferation and invasion. *Vet Comp Oncol* 2017; 15(3):718-730. <https://doi.org/10.1111/vco.12212>
56. Myzak M, Tong P, Dashwood W et al. Sulforaphane retards the growth of human PC-3 xenografts and inhibits HDAC activity in human subjects. *Exp Biol Med* (Maywood) 2007; 232(2):227-234.
57. Clarke J, Riedl K, Bella D et al. Comparison of isothiocyanate metabolite levels and histone deacetylase activity in human subjects consuming broccoli sprouts or broccoli supplement. *J Agric Food Chem* 2011; 59(20):10955-10963. <https://doi.org/10.1021/jf202887c>
58. Selting K, Sharp C, Ringold R et al. Serum 25-hydroxyvitamin D concentrations in dogs - correlation with health and cancer risk. *Vet Comp Oncol* 2016; 14(3):295-305. <https://doi.org/10.1111/vco.12101>
59. McDonnell S, Baggerly C, French C et al. Serum 25-hydroxyvitamin D concentrations ≥ 40 ng/ml are associated with >65% lower cancer risk: pooled analysis of randomized trial and prospective cohort study. *PLoS One* 2016; 11(4):e0152441. <https://doi.org/10.1023/b:verc.0000045954.71403.74>
60. Gerber B, Hauser B, Reusch C. Serum levels of 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol in dogs with hypercalcaemia. *Vet Res Commun* 2004; 28(8):669-680. <https://doi.org/10.1023/b:verc.0000045954.71403.74>
61. Wakshlag J, Rassnick K, Malone E et al. Cross-sectional study to investigate the association between vitamin D status and cutaneous mast cell tumours in Labrador retrievers. *Br J Nutr* 2011; 106 Suppl 1:S60-S63. <https://doi.org/10.1017/S000711451100211X>
62. Itariu B, Zeyda M, Leitner L et al. Treatment with n-3 polyunsaturated fatty acids overcomes the inverse association of vitamin D deficiency with inflammation in severely obese patients: a randomized controlled trial. *PLoS One* 2013; 8(1):e54634. <https://doi.org/10.1371/journal.pone.0054634>
63. Yuan L, Jiang R, Yang Y et al. 1,25-Dihydroxyvitamin D3 inhibits growth of the breast cancer cell line MCF-7 and downregulates cytochrome P4501B1 through the COX-2/PGE2 pathway. *Oncol Rep* 2012; 28(6):2131-2137. <https://doi.org/10.3892/or.2012.2031>
64. Wu X, Zhou T, Cao N et al. Role of vitamin D metabolism and activity on carcinogenesis. *Oncol Res* 2014; 22(3):129-137. <https://doi.org/10.3727/096504015X14267282610894>
65. Hershey B. Integrative therapies for palliative care of the veterinary cancer patient. *Hospice and Palliative Care for Companion Animals: Principles and Practice* 2nd Ed. Shanan A, Pierce J, Shearer T (eds). Hoboken, NJ: Wiley-Blackwell 2023:138-162.
66. Skorupski K, Hammond G, Irish A et al. Prospective randomized clinical trial assessing the efficacy of Denamarin for prevention of CCNU-induced hepatopathy in tumor-bearing dogs. *J Vet Intern Med* 2011; 25(4):838-845. <https://doi.org/10.1111/j.1939-1676.2011.0743.x>
67. Landsberg G, Nichol J, Araujo J. Cognitive dysfunction syndrome: a disease of canine and feline brain aging. *Vet Clin North Am Small Anim Pract* 2012; 42(4):749-768. <https://doi.org/10.1016/j.cvsm.2012.04.003>
68. Kidd P, Head K. A review of the bioavailability and clinical efficacy of milk thistle phytosome: a silybin-phosphatidylcholine complex (Siliphos). *Altern Med Rev* 2005; 10(3):193-203.
69. Vail D, Chun R, Thamm D et al. Efficacy of pyridoxine to ameliorate the cutaneous toxicity associated with doxorubicin containing pegylated (Stealth) liposomes: a randomized, double-blind clinical trial using a canine model. *Clin Cancer Res* 1998; 4(6):1567-1571.
70. Li X, Chen M, Huang B et al. Pyridoxine is effective for preventing hand-foot syndrome induced by pegylated liposomal doxorubicin for multiple myeloma: the results of a randomized study. *Integr Cancer Ther* 2022; 21:15347354221140402. <https://doi.org/10.1177/15347354221140402>
71. Thériault O, Poulin H, Thomas G et al. Pyridoxal-5'-phosphate (MC-1), a vitamin B6 derivative, inhibits expressed P2X receptors. *Can J Physiol Pharmacol* 2014; 92(3):189-196. <https://doi.org/10.1139/cjpp-2013-0404>
72. Raditic D, Gaylord L. Supplements for small animal cancer patients. *Today's Veterinary Practice* 2021; 11(2):26-30. <https://todaysveterinarypractice.com/nutrition/supplements-for-small-animal-cancer-patients/>
73. Yu A, Li L. The potential role of probiotics in cancer prevention and treatment. *Nutr Cancer* 2016; 68(4):535-544. <https://doi.org/10.1080/01635581.2016.1158300>
74. Chen S, Wang J, Fang Q et al. A polysaccharide from natural *Cordyceps sinensis* regulates the intestinal immunity and gut microbiota in mice with cyclophosphamide-induced intestinal injury. *Food Funct* 2021; 12(14):6271-6282. <https://doi.org/10.1039/d1fo00596k>
75. Jugan M, Wouda R, Higginbotham M. Preliminary evaluation of probiotic effects on gastrointestinal signs in dogs with multicentric lymphoma undergoing multi-agent chemotherapy: A randomised, placebo-controlled study. *Vet Rec Open* 2021; 8(1):e2. <https://doi.org/10.1002/vro.2.2>
76. Liu C, Chen W, Wang M et al. *Dendrobium officinale* Kimura et Migo and American ginseng mixture: A Chinese herbal formulation for gut microbiota modulation. *Chin J Nat Med* 2020; 18(6):446-459. [https://doi.org/10.1016/S1875-5364\(20\)30052-2](https://doi.org/10.1016/S1875-5364(20)30052-2)
77. Yang S. *The Divine Farmer's Materia Medica: A Translation of the Shen Nong Ben Cao Jing*. Boulder, CO: Blue Poppy Press 1998:25, 65, 79, 65, 137, 138, 141, 147.
78. Xie H, Preast V. *Xie's Chinese Veterinary Herbology*. Ames, IA: Wiley-Blackwell 2010:71, 72, 51, 52, 50, 51, 109, 110, 139, 140, 447, 448, 225, 226, 148, 149, 171, 172, 245, 246.
79. Das G, Shin H, Leyva-Gómez G et al. *Cordyceps* spp.: A review on its immune-stimulatory and other biological potentials. *Front Pharmacol* 2021; 11:602364. <https://doi.org/10.3389/fphar.2020.602364>
80. Li X, Yang G, Li X et al. Traditional Chinese medicine in cancer care: a review of controlled clinical studies published in Chinese. *PLoS One* 2013; 8(4):e60338. <https://doi.org/10.1371/journal.pone.0060338>
81. Li P, Cheng Z, Du X. *Management of Cancer with Chinese Medicine*. St. Albans, United Kingdom: Donica Publishing 2003:3-8, 357.
82. Ho Z. Principles of diet therapy in ancient Chinese medicine: 'Huang Di Nei Jing'. *Asia Pac J Clin Nutr* 1993; 2(2):91-95.
83. Liu J, Wang S, Zhang Y et al. Traditional Chinese medicine and cancer: History, present situation, and development. *Thorac Cancer* 2015; 6(5):561-569. <https://doi.org/10.1111/1759-7714.12270>
84. Wang Z, Chen P, Xie P. *History and Development of Traditional Chinese Medicine*. Beijing, China: Science Press 1999:102-105.
85. Maciocia G. *The Foundations of Chinese Medicine: A Comprehensive Text for Acupuncturists and Herbalists* 2nd Ed. Edinburgh, United Kingdom: Elsevier Churchill Livingstone 2005:1082, 1080, 568-571, 387-389, 448, 449.
86. Xie H, Preast V. *Xie's Veterinary Acupuncture*. Ames, IA: Blackwell Publishing 2007:202, 203, 274-276.
87. Jordan P, Wedemeyer L. *Cancer and oncology: A TCVM review. Practical Guide to Traditional Chinese Veterinary Medicine: Small Animal Practice*. Xie H, Wedemeyer L, Chrisman C, Trevisanello L (eds). Reddick, FL: Chi Institute Press 2014:575-626.
88. Hu B, Du Q, Shen K et al. Principles and scientific basis of traditional Chinese medicine in cancer treatment. *J Bioanal Biomed* 2012; S6:005. <https://doi.org/10.4172/1948-593X.S6-005>
89. Lahans T. *Integrating Conventional and Chinese Medicine in Cancer Care: A Clinical Guide*. Edinburgh, United Kingdom: Elsevier Churchill Livingstone 2007:235, 236.
90. Li G, Yang S, Li J. *Li Dong-Yuan's Treatise on the Spleen & Stomach: A Translation of the Pi Wei Lun* 2nd Ed. Boulder, CO: Blue Poppy Press 2004:3-12.
91. Koh R. Traditional Chinese veterinary medicine for cognitive dysfunction syndrome. *Am J Trad Chin Vet Med* 2018; 13(1):65-78. <https://doi.org/10.59565/UBLK2287>
92. Ferguson B. The importance of Bian Zheng (Pattern Differentiation) in TCVM. *Am J Trad Chin Vet Med* 2008; 3(1):66-73. <https://doi.org/10.59565/FZSP4218>
93. Brown D, Reetz J. Single agent polysaccharopeptide delays metastases and improves survival in naturally occurring hemangiosarcoma. *Evid Based Complement Alternat Med* 2012; 2012:384301. <https://doi.org/10.1155/2012/384301>
94. Habtemariam S. *Trametes versicolor* (synn. *Coriolus versicolor*) polysaccharides in cancer therapy: targets and efficacy. *Biomedicines* 2020; 8(5):135. <https://doi.org/10.3390/biomedicines8050135>

95. Gedney A, Salah P, Mahoney J et al. Evaluation of the anti-tumour activity of *Coriolus versicolor* polysaccharopeptide (I'm-Yunity) alone or in combination with doxorubicin for canine splenic hemangiosarcoma. *Vet Comp Oncol* 2022; 20(3):688-696. <https://doi.org/10.1111/vco.12823>
96. Ciepluch B, Wilson-Robles H, Pashmakova M et al. Long-term postoperative effects of administration of allogeneic blood products in 104 dogs with hemangiosarcoma. *Vet Surg* 2018; 47(8):1039-1045. <https://doi.org/10.1111/vsu.12967>
97. Yao Q, Chang B, Chen R et al. Research advances in pharmacology, safety, and clinical applications of Yunnan Baiyao, a traditional Chinese medicine formula. *Front Pharmacol* 2021; 12:773185. <https://doi.org/10.3389/fphar.2021.773185>
98. Wang C, Xie J, Zhang B et al. Chemopreventive effects of Panax notoginseng and its major constituents on SW480 human colorectal cancer cells. *Int J Oncol* 2007; 31(5):1149-1156.
99. Wirth K, Kow K, Salute M et al. In vitro effects of Yunnan Baiyao on canine hemangiosarcoma cell lines. *Vet Comp Oncol* 2016; 14(3):281-294. <https://doi.org/10.1111/vco.12100>
100. Murphy L, Panek C, Bianco D et al. Use of Yunnan Baiyao and epsilon aminocaproic acid in dogs with right atrial masses and pericardial effusion. *J Vet Emerg Crit Care (San Antonio)* 2017; 27(1):121-126. <https://doi.org/10.1111/vec.12529>
101. Han Y, Shen K, Yang J. Anti-metastasis effect of "Wei Chang An Decoction" on postoperative gastric cancer in Beagle dogs. *Acta Universitatis Traditionis Medicinalis Sinensis Pharmacologiaeque Shanghai* 2008; 22(04):65-68. (in Chinese). <https://doi.org/10.1010.3969/j.issn.1008-861X.2008.04.017>
102. Xu Y, Zhao A, Li Z et al. Survival benefit of traditional Chinese herbal medicine (a herbal formula for invigorating Spleen) for patients with advanced gastric cancer. *Integr Cancer Ther* 2013; 12(5):414-422. <https://doi.org/10.1177/1534735412450512>
103. Saeed M, Breuer E, Hegazy M et al. Retrospective study of small pet tumors treated with *Artemisia annua* and iron. *Int J Oncol* 2020; 56(1):123-138. <https://doi.org/10.3892/ijo.2019.4921>
104. Weathers P, Reed K, Hassanali A et al. Whole plant approaches to therapeutic use of *Artemisia annua* L. (Asteraceae). *Artemisia annua - Pharmacology and Biotechnology*. Aftab T, Ferreira J, Khan M et al. (eds). Berlin, Germany: Springer 2014:51-74.
105. Sarolri R, Andreani G, Bernardini C et al. Anticancer activity of an *Artemisia annua* L. hydroalcoholic extract on canine osteosarcoma cell lines. *Res Vet Sci* 2022; 152:476-484. <https://doi.org/10.1016/j.rvsc.2022.09.012>
106. Isani G, Bertocchi M, Andreani G et al. Cytotoxic effects of *Artemisia annua* L. and pure artemisinin on the D-17 canine osteosarcoma cell line. *Oxid Med Cell Longev* 2019; 2019:1615758. <https://doi.org/10.1155/2019/1615758>
107. Xie H, Hershey B, Ma A. Review of evidence-based clinical and experimental research on the use of acupuncture and Chinese herbal medicine for the treatment or adjunct treatment of cancer. *Am J Trad Chin Vet Med* 2017; 12(1):69-77. <https://doi.org/10.59565/001c.128181>
108. Wen J, Johnston K. Long-term follow-up of canine mammary gland neoplasia in eight dogs treated with surgery and a new Chinese herbal formula. *Am J Trad Chin Vet Med* 2011; 6(1):27-31. <https://doi.org/10.59565/001c.128185>
109. Chen S, Qin X, Jin S et al. The comparative study on the antitumor effects of Xihuang pills, Frankincense, Myrrh, and combination of Frankincense and Myrrh on diverse human malignant tumor cells in vitro. *Pharmacology and Clinics of Chinese Materia Medica* 2016; 32(3):102-104. (in Chinese).
110. Hao J, Jin Z, Zhu H et al. Antiestrogenic activity of the Xi-Huang formula for breast cancer by targeting the estrogen receptor α . *Cell Physiol Biochem* 2018; 47(6):2199-2215. <https://doi.org/10.1159/000491533>
111. Shahrajabian M, Sun W, Cheng Q. Clinical aspects and health benefits of ginger (*Zingiber officinale*) in both traditional Chinese medicine and modern industry. *Acta Agriculturae Scandinavica, Section B — Soil & Plant Science* 2019; 69(6):546-556. <https://doi.org/10.1080/09064710.2019.1606930>
112. Zhao Y, Dai Y, Nie K. Research progress on the antiemetic effect of traditional Chinese medicine against chemotherapy-induced nausea and vomiting: a review. *Front Pharmacol* 2022; 12:790784. <https://doi.org/10.3389/fphar.2021.790784>
113. Konmun J, Danwilai K, Ngamphaiboon N et al. A phase II randomized double-blind placebo-controlled study of 6-gingerol as an anti-emetic in solid tumor patients receiving moderately to highly emetogenic chemotherapy. *Med Oncol* 2017; 34(4):69. <https://doi.org/10.1007/s12032-017-0931-4>
114. Sharma S, Kochupillai V, Gupta S et al. Antiemetic efficacy of ginger (*Zingiber officinale*) against cisplatin-induced emesis in dogs. *J Ethnopharmacol* 1997; 57(2):93-96. [https://doi.org/10.1016/s0378-8741\(97\)00054-8](https://doi.org/10.1016/s0378-8741(97)00054-8)
115. Ai X, Yu P, Li X et al. Polysaccharides from *Spirulina platensis*: Extraction methods, structural features and bioactivities diversity. *Int J Biol Macromol* 2023; 231:123211. <https://doi.org/10.1016/j.ijbiomac.2023.123211>
116. Huang Z, Wang C, Chen J et al. Ameliorating effect on glycolipid metabolism of *Spirulina* functional formulation combination from traditional Chinese medicine. *Oxid Med Cell Longev* 2022; 2022:3910116. <https://doi.org/10.1155/2022/3910116>
117. Zhang H, Lin A, Sun Y et al. Chemo- and radio-protective effects of polysaccharide of *Spirulina platensis* on hemopoietic system of mice and dogs. *Acta Pharmacol Sin* 2001; 22(12):1121-1124.
118. Satyaraj E, Reynolds A, Engler R et al. Supplementation of diets with *Spirulina* influences immune and gut function in dogs. *Front Nutr* 2021; 8:667072. <https://doi.org/10.3389/fnut.2021.667072>
119. Cai B, Zhao X, Luo L et al. Structural characterization, and in vitro immunostimulatory and antitumor activity of an acid polysaccharide from *Spirulina platensis*. *Int J Biol Macromol* 2022; 196:46-53. <https://doi.org/10.1016/j.ijbiomac.2021.12.062>
120. Zhang C, Suzuki T, Yoshie Y. 沙虫干呈味及功能性成分研究 [Study on tasty substance and functional components of the dried sha chong (*Sipunculus nudus*)]. *Journal of Guangdong Ocean University* 2000; 20(2):24-27. (in Chinese). <https://doi.org/10.3969/j.issn.1673-9159.2000.02.006>
121. Zhang C, Dai Z, Cai Q. Anti-inflammatory and anti-nociceptive activities of *Sipunculus nudus* L. extract. *J Ethnopharmacol* 2011; 137(3):1177-1182. <https://doi.org/10.1016/j.jep.2011.07.039>
122. Ge Y, Tang Y, Guo S et al. Simultaneous quantitation of free amino acids, nucleosides and nucleobases in *Sipunculus nudus* by ultra-high performance liquid chromatography with triple quadrupole mass spectrometry. *Molecules* 2016; 21(4):408. <https://doi.org/10.3390/molecules21040408>
123. Cui F, Li M, Chen Y et al. Protective effects of polysaccharides from *Sipunculus nudus* on Beagle dogs exposed to γ -radiation. *PLoS One* 2014; 9(8):e104299. <https://doi.org/10.1371/journal.pone.0104299>
124. Li N, Shen X, Liu Y et al. Isolation, characterization, and radiation protection of *Sipunculus nudus* L. polysaccharide. *Int J Biol Macromol* 2016; 83:288-296. <https://doi.org/10.1016/j.ijbiomac.2015.11.071>
125. Su J, Liao D, Su Y et al. Novel polysaccharide extracted from *Sipunculus nudus* inhibits HepG2 tumour growth in vivo by enhancing immune function and inducing tumour cell apoptosis. *J Cell Mol Med* 2021; 25(17):8338-8351. <https://doi.org/10.1111/jcmm.16793>
126. Jordan J, Nowak A, Lee T. Activation of innate immunity to reduce lung metastases in breast cancer. *Cancer Immunol Immunother* 2010; 59(5):789-797. <https://doi.org/10.1007/s00262-009-0800-x>
127. Lee K, Morris-Natschke S, Yang X et al. Recent progress of research on medicinal mushrooms, foods, and other herbal products used in traditional Chinese medicine. *J Tradit Complement Med* 2012; 2(2):84-95.
128. Liu W, Chuang W, Tsai M et al. *Cordyceps sinensis* health supplement enhances recovery from taxol-induced leukopenia. *Exp Biol Med (Maywood)* 2008; 233(4):447-455. <https://doi.org/10.3181/0708-RM-230>
129. Liu Y, Wang J, Wang W et al. The chemical constituents and pharmacological actions of *Cordyceps sinensis*. *Evid Based Complement Alternat Med* 2015; 2015:575063. <https://doi.org/10.1155/2015/575063>
130. Gianotti B, Cleaver M, Mullins M et al. Preclinical evaluation of concurrent medicinal mushroom-based immune-enhancement supplementation in dogs undergoing chemotherapy for various cancers. *Int J Med Mushrooms* 2009; 11(2):167-184. <https://doi.org/10.1615/IntJMedMushr.v11.i2.60>

131. Wu Q, Liang X. Food therapy and medical diet therapy of traditional Chinese medicine. *Clin Nutr Exper* 2018; 18:1-5. <https://doi.org/10.1016/j.yclnex.2018.01.001>
132. Fowler M. Traditional Chinese veterinary medicine to treat Kidney Jing deficiency with emphasis on food therapy and Chinese herbal medicine. *Am J Trad Chin Vet Med* 2020; 15(2):67-72. <https://doi.org/10.59565/ZTPL5976>
133. Xie H, Preast V. *Traditional Chinese Veterinary Medicine: Fundamental Principals 2nd Ed.* Reddick, FL: Chi Institute Press 2013:311, 312, 186, 187, 407, 408.
134. Paul S, Emran T, Saha D et al. Phytochemical and antimicrobial activity of the plant extracts of Brassica oleracea against selected microbes. *Asian Journal of Pharmacy and Medical Science* 2012; 2(2):30-34.
135. DiNatale C. Cancer treatment in geriatric animals. *Am J Trad Chin Vet Med* 2012; 7(2):55-66. <https://doi.org/10.59565/NIJW4255>
136. Pitchford P. *Healing with Whole Foods: Asian Traditions and Modern Nutrition 3rd Ed.* Berkeley, CA: North Atlantic Books 2002:537, 538, 541, 314, 327.
137. Kastner J. *Chinese Nutrition Therapy: Dietetics in Traditional Chinese Medicine (TCM) 2nd Ed.* Stuttgart, Germany: Georg Thieme Verlag 2009:46, 144, 156.
138. Morgan J. Chinese food therapy for the veterinary clinic. *IVC Journal* 2016; 6(3):60-62.
139. Wicke R, Cheung C. Principles for applying traditional Chinese medicine to cases of cancer. *Integr Cancer Ther* 2002; 1(2):175-178. <https://doi.org/10.1177/1534735402001002009>
140. Chiang E, Oberste J, Tran H et al. Chinese medicine oncology & immunology: colorectal cancer, a case study. *The Journal of Acupuncture & Integrative Medicine* 2023; 31(1):7-16.
141. Liang P, Chen X, Gong M et al. Guang Chen Pi (the pericarp of Citrus reticulata Blanco's cultivars 'Chachi') inhibits macrophage-derived foam cell formation. *J Ethnopharmacol* 2022; 293:115328.
142. Flaws B. *The Tao of Healthy Eating: Dietary Wisdom According to Chinese Medicine.* Boulder CO: Blue Poppy Press 1998:78, 95.
143. Lu H. *Chinese Natural Cures: Traditional Methods for Remedies and Prevention.* New York, NY: Black Dog & Leventhal Publishers 1999:332.
144. Zhang Y, Liang Y, He C. Anticancer activities and mechanisms of heat-clearing and detoxicating traditional Chinese herbal medicine. *Chin Med* 2017; 12:20. <https://doi.org/10.1186/s13020-017-0140-2>
145. Xu H, Xu H. Chinese food and cancer healing. *Integrative Medicine Insights* 2006; 1:1-5. <https://doi.org/10.1177/117863370600100001>
146. Wang H, Khor T, Shu L et al. Plants vs. cancer: a review on natural phytochemicals in preventing and treating cancers and their druggability. *Anticancer Agents Med Chem* 2012; 12(10):1281-1305. <https://doi.org/10.2174/187152012803833026>
147. Ubago-Guisado E, Rodríguez-Barranco M, Ching-López A et al. Evidence update on the relationship between diet and the most common cancers from the European Prospective Investigation into Cancer and Nutrition (EPIC) study: a systematic review. *Nutrients* 2021; 13(10):3582. <https://doi.org/10.3390/nu13103582>
148. Long J, Ji Z, Yuan P et al. Nut consumption and risk of cancer: a meta-analysis of prospective studies. *Cancer Epidemiol Biomarkers Prev* 2020; 29(3):565-573. <https://doi.org/10.1158/1055-9965.EPI-19-1167>
149. Gaesser G. Whole grains, refined grains, and cancer risk: a systematic review of meta-analyses of observational studies. *Nutrients* 2020; 12(12):3756. <https://doi.org/10.3390/nu12123756>
150. Wang Y, Liu K, Long T et al. Dietary fish and omega-3 polyunsaturated fatty acids intake and cancer survival: A systematic review and meta-analysis. *Crit Rev Food Sci Nutr* 2023; 63(23):6235-6251. <https://doi.org/10.1080/10408398.2022.2029826>
151. Boutas I, Kontogeorgi A, Dimitrakakis C et al. Soy isoflavones and breast cancer risk: a meta-analysis. *In Vivo* 2022; 36(2):556-562. <https://doi.org/10.21873/invivo.12737>
152. Zamani F, Khalighfard S, Kalhori M et al. Expanding CYLD protein in NF- κ B/TNF- α signaling pathway in response to Lactobacillus acidophilus in non-metastatic rectal cancer patients. *Med Oncol* 2023; 40(10):302. <https://doi.org/10.1007/s12032-023-02170-y>
153. Han X, Zheng T, Foss F et al. Vegetable and fruit intake and non-Hodgkin lymphoma survival in Connecticut women. *Leuk Lymphoma* 2010; 51(6):1047-1054. <https://doi.org/10.3109/10428191003690364>
154. Chagas T, Borges D, de Oliveira P et al. Oral fish oil positively influences nutritional-inflammatory risk in patients with haematological malignancies during chemotherapy with an impact on long-term survival: a randomised clinical trial. *J Hum Nutr Diet* 2017; 30(6):681-692. <https://doi.org/10.1111/jhn.12471>
155. Mei J, Qian M, Hou Y et al. Association of saturated fatty acids with cancer risk: a systematic review and meta-analysis. *Lipids Health Dis* 2024; 23(1):32. <https://doi.org/10.1186/s12944-024-02025-z>
156. Owens E, Harris L, Harris A et al. The gene expression profile and cell of origin of canine peripheral T-cell lymphoma. *BMC Cancer* 2024; 24(1):18. <https://doi.org/10.1186/s12885-023-11762-w>
157. Oh J, Cho J. Comparative oncology: overcoming human cancer through companion animal studies. *Exp Mol Med* 2023; 55(4):725-734. <https://doi.org/10.1038/s12276-023-00977-3>
158. Hou H, Chen D, Zhang K et al. Gut microbiota-derived short-chain fatty acids and colorectal cancer: Ready for clinical translation? *Cancer Lett* 2022; 526:225-235. <https://doi.org/10.1016/j.canlet.2021.11.027>
159. Madrigal-Matute J, Bañón-Escandell S. Colorectal cancer and microbiota modulation for clinical use. a systematic review. *Nutr Cancer* 2023; 75(1):123-139. <https://doi.org/10.1080/01635581.2022.2108468>
160. Fusco W, Lorenzo M, Cintoni M et al. Short-chain fatty-acid-producing bacteria: key components of the human gut microbiota. *Nutrients* 2023; 15(9):2211. <https://doi.org/10.3390/nu15092211>
161. Zhu D, Jiang N, Wang N et al. A literature review of the pharmacological effects of jujube. *Foods* 2024; 13(2):193. <https://doi.org/10.3390/foods13020193>
162. Tahergorabi Z, Abedini M, Mitra M et al. "Ziziphus jujuba": A red fruit with promising anticancer activities. *Pharmacogn Rev* 2015; 9(18):99-106. <https://doi.org/10.4103/0973-7847.162108>
163. Shi H, Zhu W, Yuan Y et al. Introducing Chinese food therapy: A review of origin, developing course and modern application. *TMR Integrat Nurs* 2018; 2(2):42-48. <https://doi.org/10.53388/TMRIN20180301>
164. Shen C, Pang S, Kwong E et al. The effect of Chinese food therapy on community dwelling Chinese hypertensive patients with Yin-deficiency. *J Clin Nurs* 2010; 19(7-8):1008-1020. <https://doi.org/10.1111/j.1365-2702.2009.02937.x>